BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 27 1951

THE METABOLISM OF HISTAMINE*

BY

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A lecture on histamine published three years ago (Gaddum, 1948) showed that, in spite of much work, there were many gaps in our knowledge of this substance. Since that time some progress has been made, but there is still much that we do not know. We do not know whether histamine is to be regarded as an essential part of the normal machinery without which the body would not work, or whether it is a substance which appears only as part of the response to injury. We know that the body of a cat, for example, contains enough histamine to kill the cat, but we do not know why it does not normally do so. We imagine that the histamine must be stored in combination with something else which inactivates it, and suggestions have been made about how this is done, but no one has isolated the compound which we imagine to be formed. We do not know where the body histamine is formed or why some tissues contain much more than others.

The pharmacological actions of histamine can be summed up by saying that it causes a contraction of most plain muscles, a dilatation of capillaries, and secretion of most glands, and particularly of the acid-secreting glands in the stomach. There is no need to say more about these pharmacological actions, except to acknowledge our debt to the guinea-pig, whose plain muscles are so very sensitive to histamine. Most of our knowledge about the metabolism of histamine depends upon pharmacological assays using guinea-pigs' plain muscle.

Antihistamines

The antihistamines, which have done so much to attract attention to histamine in recent years, antagonize all its effects except that on the gastric juice. They may be used in evidence for or against the theory that any particular phenomenon is due to the release of histamine, but if so used they must be used with care. In addition to their actions against histamine, many antihistamines have a local anaesthetic action, actions like atropine and quinidine, and a depressant action on the central nervous system. A phenomenon which is abolished by an antihistamine may thus, for example, be due to the release of acetylcholine. Some of the antihistamines are, of course, more specific than others. The one which was originally known as "neoantergan," and has now been officially christened mepyramine, is more specific in its action against histamine than atropine is in its action against acetylcholine. If any phenomenon is abolished by mepyramine, the possibility that it is due to the release of histamine must be seriously considered, but should not be accepted without further evidence. It should also be abolished by other antihistamines more easily than by atropine, and, if possible, there should be direct evidence that abnormal amounts of histamine can be detected by suitable tests in fluids which have been in contact with stimulated tissues.

It might be thought that an effect which is not abolished by an antihistamine cannot be due to the release of histamine, and there is indeed some force in this argument. It is not, however, conclusive, as there are various nerves which are thought to act by liberating acetylcholine, although their effects are not abolished by atropine (Dale and Gaddum, 1930). This question has been discussed by Sir Henry Dale (1948), who comes to the conclusion that effects may be due to the release either of intrinsic histamine or of extrinsic histamine. The histamine is called intrinsic when it is released by the cells which give the response, as it presumably is when the plain muscle of a guinea-pig gives an anaphylactic response. The histamine is called extrinsic when it is released by one cell and acts upon another. In urticaria, for example, the histamine is thought to be released by the epithelial cells and to act upon the blood vessels. Dale suggests that effects due to extrinsic histamine are more easily abolished by antihistamines than effects due to intrinsic histamine. In the latter case, the histamine is perhaps released behind the barrier set up by the antihistamines. This theory explains some of the peculiarities of the actions of antihistamines.

With these facts in mind, it is safe to say that the antihistamines have lent strong support to the view that anaphylactic and allergic phenomena are many of them due to the release of histamine. They have also been used as evidence that various other effects are due to the release of histamine. An interesting example of this is the work of Erspamer and Paolini (1948), who have found that antihistamines inhibit the action of irritant purgatives, such as jalap and castor oil, and suggest that these substances produce their purgative effect by liberating histamine in the wall of the intestine.

Histamine in Blood

Our knowledge of the physiological and pathological roles of histamine depends largely upon experiments in which it was detected and estimated by pharmacological methods. The concentration of histamine in blood may be estimated pharmacologically, but the results have on the whole been disappointing, mainly because blood is

*A lecture delivered at the invitation of the Swedish universities.

such a complicated fluid. When human blood is centrifuged most of the histamine is found in the leucocytes. It is probably in granulocyte cells, since when these are present in the blood in very large numbers in myelogenous leukaemia the blood histamine is very high (Marcou *et al.*, 1937; Code and Macdonald, 1937). It seemed probable at one time that most of the histamine was in the eosinophil cells. The theory has now been discredited, since Rose (1950) caused a complete disappearance of eosinophils from the circulating blood by injecting the adrenocorticotrophic hormone (A.C.T.H.) without any clear effect on the blood histamine. A comparatively low concentration is normally present in the plasma, but it is doubtful whether the methods as yet available give a reliable estimate of this. Histamine added to blood *in vitro* is partly taken up by the red cells, which do not part with it easily (Anrep *et al.*, 1939). Some of those who study the release of histamine in the body estimate its concentration in the blood coming from a tissue which is expected to release it, and their results may possibly be due to the squeezing of leucocytes out of the tissue. Others estimate the concentration in the plasma, and their results may possibly be due to the disintegration of leucocytes with the liberation of histamine from these leucocytes into the plasma. When large changes are observed such things do not matter, but when smaller changes are being studied they may become important.

The experiments of Rose (1941) on anaphylaxis in rabbits provide an example of the odd results which may be obtained by estimating histamine in the blood. It is known that histamine is liberated in anaphylactic shock. It might therefore be expected that during this kind of shock histamine would disappear from the lung and spleen and appear in the blood. Rose found, on the contrary, that histamine disappeared not only from the lung and spleen but also from the blood itself. The blood cells liberated their histamine in just the same way as the lung cells and spleen cells, and he never found where the histamine went to next. Care is evidently needed in the interpretation of the results of experiments on blood histamine.

Histamine in Urine

During recent years a number of conclusions have been reached by estimating the concentration of histamine in the urine. The first clear evidence about this appeared in an interesting paper from Cairo (Anrep *et al.*, 1944). In this paper, Anrep and his colleagues described a method for concentrating histamine by adsorbing it on charcoal and so separating it from the large amounts of potassium which would otherwise interfere with pharmacological assays. They found that the urine histamine was partly free and partly conjugated. The conjugated histamine had no pharmacological activity, but became active when hydrolysed with acid. They collected urines from various animals in the Cairo zoo, including elephants, camels, water-buffaloes, anthropoid apes, lions, tigers, and leopards. These experiments showed that a diet of meat leads to the excretion of large amounts of conjugated histamine in the urine. When pure histamine was given by the mouth to dogs some of it appeared in the conjugated form in the urine; when it was injected some of it appeared as free histamine in the urine.

These interesting results have been confirmed and extended in other laboratories. Urbach (1949) used paper chromatography to separate the two forms of histamine from one another and from the other substances present in urine, and in this way he obtained evidence that conjugated histamine is acetylhistamine. There can be no doubt about this, since Tabor and Mosettig (1949) have actually isolated acetylhistamine from the urine of a dog which had been given histamine by the mouth.

Henry Adam, with various colleagues, has been studying the excretion of histamine by man, in my laboratory. At first he used Anrep's methods, adsorbing the histamine on charcoal and estimating the difference between hydrolysed and unhydrolysed samples. More recently, he has been using other absorbents and separating the two forms of histamine from one another. His results show clearly that free histamine is normally present in human urine as well as acetylhistamine.

When histamine was given by the mouth there was a large increase in the amount of conjugated histamine in the urine and a small but definite increase in the amount of free histamine. When histamine was given by slow intravenous injection there was a large increase in the amount of free histamine in the urine and no change at all in the amount of conjugated histamine (Adam, 1950; Roberts and Adam, 1950). These observations confirm those of Anrep *et al.* (1944) on dogs, and support the view that the conjugation of histamine occurs in the intestine or liver. The amount normally present in the urine depends on the diet, and varies widely. Estimations of conjugated histamine might perhaps be used as an indication of the amount of histamine in the diet, but it seems likely that care would be needed in the calculations. In the experiments on man the proportion of an oral dose of histamine recovered in the urine varied between 0.17 and 1.2%.

Free histamine is more interesting than conjugated histamine. The average amount found in 30 urines from five normal young men was 21.6 μg. per 24 hours, and the extreme values were 12 and 41 μg. The concentration in the urine is less than that in whole blood, but much greater than that in plasma. When histamine was given by slow intravenous injection there was a definite increase in the amount of free histamine in the urine, even when the rate of injection was so slow that no effects could be detected except a small secretion of acid in the stomach. By conventional methods estimates were made of the concentration of histamine in the plasma in these experiments, and no definite change was detected. The estimation of free histamine in the urine is thus the most sensitive way we know of detecting the liberation of histamine in the body. It is, of course, necessary to collect all the urine secreted during a given time; a simple estimate of concentration is likely to be too much affected by drinks.

The increase in the amount of free histamine in the urine was about 1% of the amount injected. Most of the histamine must be destroyed elsewhere in the body, and the amount escaping in the urine makes no practical difference to the rate of disappearance of histamine. It does, however, provide an indirect measure of one aspect of histamine metabolism. The percentage appearing in the urine seemed to be independent of the dose (which was never very large), so it is reasonable to assume that the amount normally present in the urine was 1% of the amount of histamine normally liberated into the blood by physiological processes. This leads to the conclusion

that free histamine was appearing in the blood stream of these young men at the rate of 2 to 3 mg. per 24 hours.

It might be suggested that this histamine came directly from the gut and represented the small amount which had escaped acetylation. This is unlikely for the following reasons. The excretion of conjugated histamine showed wide fluctuations presumably associated with the diet, but the excretion of free histamine was much more constant, and showed no tendency to increase when the excretion of conjugated histamine increased. It seems more likely that this 2 to 3 mg. of histamine is liberated into the blood from the tissues every 24 hours. It may, of course, represent only a small fraction of a much larger amount most of which is immediately destroyed by histaminase before absorption in the blood, but it does provide something to think about. The total amount of histamine liberated must be at least as much as this.

It is too soon to say much yet about the excretion of histamine in disease, but Adam *et al.* (1950) did find that the rate of excretion of free histamine was higher in patients suffering from urticaria than in other patients or in normal persons.

Little is definitely known about where the histamine in the body comes from. One theory is that it is all absorbed from the gut like a vitamin. Adam and his colleagues did, in fact, find some increases of free histamine in the urine when histamine was given by the mouth. It is, however, doubtful whether this is the main source of body histamine. We know very little about the histamine content of diets and cannot calculate with confidence how much histamine may come from this source.

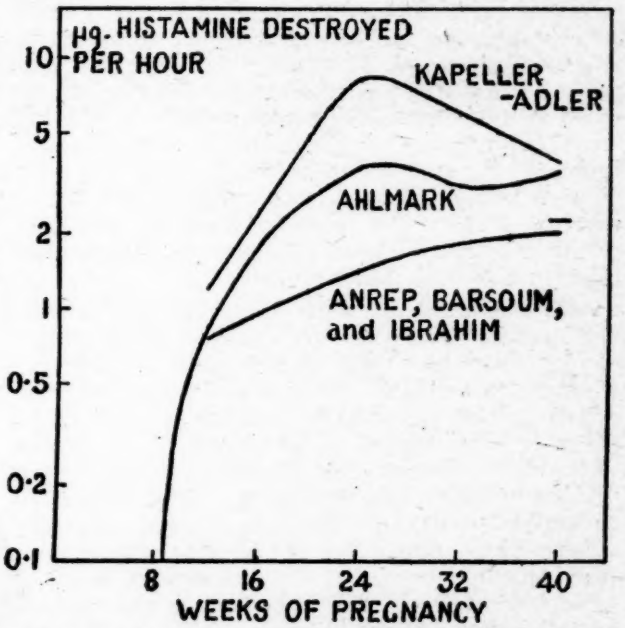
The other theory is that the histamine in the body has mostly been formed from histidine by the enzyme histidine decarboxylase. This enzyme was discovered and has been studied by Holtz (1937) and his colleagues. Blaschko (1945) has thrown doubt on its importance, since it appears to be absent in many species of animal, but the matter should be reinvestigated.

The excretion of histamine in the urine represents a very small proportion of the total histamine metabolism in man. When the body is flooded with histamine, however, the proportion may be larger, as is illustrated by some experiments by Alexander (1946), who injected 3 mg. of histamine intravenously in each of a group of mice and followed its fate by making an extract of the whole animal and estimating the total amount of histamine contained in it. The mouse is particularly adapted to such experiments, not only because of its small size, but also because of its great resistance to histamine. In these experiments about 1 mg. of histamine appeared in the urine, and the other 2 mg. was destroyed by the mouse within 24 hours.

Histaminase

Most of the histamine is presumably destroyed by the enzyme histaminase, which was discovered by Best (1929) and has recently been studied extensively in Sweden. Our knowledge of its distribution in the body is fragmentary. According to Best and McHenry (1930), particularly high concentrations are found in the kidneys and intestines of dogs. In Carlsten's (1950) interesting experiments on cats in Lund, lymph from the kidneys and intestines also appeared to be particularly rich in histaminase, but the enzyme was not found in the kidneys of rats or guinea-pigs (McHenry and Gavin, 1931) or rabbits (Anrep *et al.*, 1936). In rats it is found in the lungs, and the amount present is not increased by the repeated administration of histamine (Rose *et al.*, 1940). The distribution of the enzyme seems to be different in different species. The fact that it is found in the lymph suggests that it may move about from one part of the body to another. The fact that adrenalectomy increases the amount in the lymph suggests that the distribution of this enzyme in the body may depend upon the state of the adrenal glands and, possibly, upon other experimental conditions.

Estimates of histaminase are being made by several different methods, and it is difficult to compare the results because the conditions are not always the same. This may be illustrated by comparing three curves showing estimates of the histaminase in blood throughout



Estimates of histaminase in serum or plasma during pregnancy. Different methods give different results.

pregnancy. In each case the result is expressed in the Chart as the amount of histamine destroyed per hour. The middle curve represents the results of Ahlmark (1944). The lower curve shows earlier results obtained by a similar method in Egypt. It might be thought that these results showed that Egyptian bloods contained less enzyme than Swedish bloods. Actually, the difference is probably due to the fact that less histamine was used in the Egyptian experiments, in which the maximum possible rate corresponding to complete destruction of all the histamine was 2.2 μg. per ml. per hour.

The upper curve shows results obtained by a method recently developed in my laboratory by Mrs. Kapeller-Adler (1951a). In this method the enzyme is incubated with histamine and indigo carmine for 24 hours in the presence of chloroform. The indigo carmine is partly decolorized by H_2O_2 liberated by the action of the enzyme on the histamine, and the result depends on measuring the amount of permanganate necessary to decolorize the rest of the dye. This method is not so sensitive as the biological methods, but is accurate and sensitive enough to estimate the histaminase in blood after the eighth week of pregnancy. It has the advantage that it avoids the use of bioassay. It is no more

difficult than the estimation of phosphatase, and is likely to be popular for this reason. The results in terms of histamine destroyed tend to be higher than those obtained by other methods.

There is danger of confusion in the estimation of histamine. Consider the effect of the concentration of histamine during incubation, which varies between 0.17 and 150 μg. per ml. in different methods, and may even vary as much as fivefold in different experiments with the same method. With most enzymes the effect of changing the concentration of the substrate may be expressed approximately by the equation of Michaelis. At a certain critical concentration, defined by the Michaelis constant, the rate is half the maximal rate. At concentrations much higher than this the rate is independent of the concentration of the substrate, while at lower concentrations it is proportional to the concentration of the substrate. For consistent results, either the concentration must be well above the critical figure or it must be very rigidly standardized. The published figures for the Michaelis constant of histaminase correspond to concentrations of between 50 and 90 mg. per litre. These figures are probably higher than the real figure, but the concentrations actually used are almost certainly below the critical concentration. This can be seen clearly from the results of Best and McHenry (1930). The concentration of histamine should be more rigidly standardized than it is.

According to Mrs. Kapeller-Adler, the rate of destruction of histamine is increased by oxygen, by flavine-adenine dinucleotide, and by oestrogens. Such factors will have to be taken into account before we have a perfect method of estimating histaminase. Her results for the concentration of histaminase in the serum throughout pregnancy seem to show, in the first place, that the concentration of histaminase, as measured by her method, tends to be low in pre-eclamptic toxaemia. Other workers, using other methods, do not agree about this. She also found that the concentration was high when there were twins. All her results are consistent with the view that the amount of histaminase in the plasma is directly proportional to the amount of living placental tissue in the uterus. Since it is generally agreed that the histaminase comes from the placenta (Swanberg, 1950), this is not a surprising conclusion.

There is no general agreement about the specificity of histaminase. Preparations of this enzyme oxidize the diamines putrescine and cadaverine as well as histamine, and their rates of action on the three substrates are similarly affected by drugs and by changes of *p*H. The effect of serum on all three substrates is increased during pregnancy. The presence of cadaverine inhibits the rate of inactivation of histamine (Kapeller-Adler, 1949). These facts all support the theory of Zeller according to which the enzyme which inactivates histamine also acts on diamines in general and should be called diamin-oxidase.

On the other hand, there is evidence that this theory is too simple :

1. When the purified enzyme is dialysed its action on histamine decreases, while that on cadaverine, etc., increases. Both these changes seem to be due to the loss of flavine-adenine dinucleotide (F.A.D.), which reverses them (Kapeller-Adler, 1949). Oestrogens appear to act like F.A.D. (Kapeller-Adler, 1951b).

2. The ratio of the effect on histamine to that on cadaverine is high for purified enzyme from hog's kidney and low for the serum of pregnant women, especially if they are suffering from pre-eclamptic toxaemia (Kapeller-Adler, 1951a).

3. The enzyme has no effect on diamines in which the two amino groups are separated by a straight chain of more than eight carbon atoms (Blaschko, 1949).

The moral of all this is that the term diaminoxidase should be avoided for the present.

It is clear that much remains to be done with histaminase. Its general importance is emphasized by some experiments by Mongar and Schild (1951), who found that various substances which poison histaminase produced an increase in the effect of histamine on a piece of plain muscle isolated from the body and suspended in a bath. These observations suggest that the enzyme is present at the site where the histamine acts in sufficient concentration to destroy histamine more rapidly than it can diffuse in from outside, and that histaminase controls the action of histamine in the same sort of way that cholinesterase controls the actions of acetylcholine. Our methods of detecting and estimating histaminase are not very sensitive, and it seems likely that it is much more widely distributed in the tissues than our present evidence would suggest. It does not act very rapidly, and it is possible that it is normally in action all the time, and that the histamine content of tissues represents a balance between production and destruction.

Allergy

Consider now the phenomena of anaphylaxis and allergy. It is agreed by most people that anaphylaxis is due to the combination of antigen with antibody inside cells, which damages the cells and may lead to the release not only of histamine but also of various other toxic substances. It is also generally agreed that allergy is very similar to anaphylaxis, and that allergic urticaria, for example, is due to the release of histamine. There was little doubt about this even before the introduction of antihistamines. The successful use of these drugs in the treatment of urticaria has settled the question. The allergic response is primarily due to the mechanism which produces anaphylaxis, but this does not explain why some people are allergic and some are not. There must be some biochemical peculiarity which distinguishes allergic people from normal people. Their condition might be due either to the liberation of abnormally large amounts of histamine or to an abnormal sensitivity to histamine. It is perhaps surprising to find that there is evidence in favour of both these theories.

Evidence of an abnormal release of histamine was obtained by Katz and Cohen (1941), who incubated blood from allergic patients with various allergens and showed that the allergen to which the patient was susceptible released histamine from the blood cells into the plasma. Hawkins *et al.* (1951) have recently obtained similar results with fragments of lung removed from allergic patients. Serafini (1948) observed a brief rise of blood histamine when horse dander was injected intradermally in 54 places at once in a sensitive patient. The finding of abnormal quantities of histamine in the urine of allergic patients by Adam *et al.* has already been mentioned. All these results show that allergic patients release abnormal amounts of histamine.

It seems to be generally agreed also that allergic patients are abnormally sensitive to histamine. When given by intravenous injection this substance causes flushing of the face and neck in everyone, but allergic

manifestations such as asthma, urticaria and changes in the nasal mucous membrane occur only in persons who are liable to suffer from such complaints (Weiss *et al.*, 1932 ; Rose, 1947).

Both sets of facts can be explained on the theory that allergic patients are deficient in histaminase. This would mean that any histamine released on injury would be more likely to escape into the circulation and be detected by the experimenter. It might mean that the tissues contained more histamine than those of normal persons, and so had more histamine to release when injured. A deficiency of histaminase would also be expected to make the tissues more sensitive to histamine, as it did when Mongar and Schild poisoned the enzyme with suitable drugs. This deficiency might be localized in the skin in urticaria and in the nasal mucous membrane in hay-fever. A deficiency of histaminase and an excess of histamine in the tissues might be expected to diminish the rate of disappearance of histamine in the body.

Serafini and his colleagues in Rome (Serafini, 1948 ; Frugoni and Serafini, 1950) have obtained some evidence of this by constructing what they call histamine-tolerance curves. Histamine is injected subcutaneously in a dose of 1 mg. and its concentration is estimated in eight samples of blood collected during the next 20 minutes. In normal persons no changes are detected in the blood histamine, but in asthmatics it is found to rise to a maximum value in three minutes and to remain high for about 15 minutes. On the other hand, Jiménez Díaz *et al.* (1950) failed to confirm these results, and Adam *et al.* (1950) found no clear difference between allergic patients and normal persons when they estimated the percentage of an intravenous dose which appeared in the urine.

It is clear that some of the evidence is conflicting, but the theory that a deficiency of histaminase in the tissues plays a part in the causation of allergy appears to deserve serious consideration. This theory may perhaps have been in the minds of those who sought to treat allergy by the injection of histaminase (see Feinberg, 1946). The failure of this treatment does not disprove the theory.

Summary

Work on antihistamines has emphasized the importance of histamine itself and drawn attention to many gaps in our knowledge. Changes in the total blood histamine are difficult to interpret, as histamine is normally present in the leucocytes, and the available methods do not give a reliable estimate of plasma histamine unless this is much increased above the normal value.

The urine normally contains free histamine and the inactive substance acetylhistamine. The amount of free histamine excreted by man is normally about 20 μg. per 24 hours. This is increased after intravenous injections of histamine and may be increased during allergic attacks. The amount of acetylhistamine can be increased by giving histamine orally. Estimates of this substance are of comparatively little interest at present.

The normal fate of most of the histamine in the body is to be destroyed by the enzyme histaminase, which should retain its original name and not be called diaminoxidase. The discovery that substances which poison histaminase may sensitize tissues to histamine suggests that this enzyme plays a part in the body similar to that of cholinesterase.

In allergy the tissues not only release abnormal amounts of histamine but are also abnormally sensitive to this substance. Both these facts can be explained on the theory that those tissues which give an allergic response are deficient in histaminase.

References

Adam, H. M. (1950). *Quart. J. exp. Physiol.*, **35**, 281.
—— Hunter, R. B., and Kinnear, T. W. G. (1950). Ibid., **36**, 49.
Ahlmark, A. (1944). *Acta physiol. scand.*, **9**, Suppl. 28.
Alexander, F. (1946). *Quart. J. exp. Physiol.*, **33**, 71.
Anrep, G. V., Ayadi, M. S., Barsoum, G. S., Smith, J. R., and Talaat, M. M. (1944). *J. Physiol.*, **103**, 155.
—— Barsoum, G. S., and Talaat, M. (1936). Ibid., **86**, 55P.
—— —— —— and Wieninger, E. (1939). Ibid., **96**, 130.
Best, C. H. (1929). Ibid., **67**, 256.
—— and McHenry, E. W. (1930). Ibid., **70**, 349.
Blaschko, H. (1945). *Advanc. Enzymol.*, **5**, 67.
—— (1949). *Proc. 1st int. Congr. Biochem., Cambridge*, p. 565.
Carlsten, A. (1950). *Acta physiol. scand.*, **20**, Suppl. 70, p. 5.
Code, C. F., and Macdonald, A. D. (1937). *Lancet*, **2**, 730.
Dale, H. H. (1948). *British Medical Journal*, **2**, 281.
—— and Gaddum, J. H. (1930). *J. Physiol.*, **70**, 109.
Erspamer, V., and Paolini, A. (1948). *Arch. int. Pharmacodyn.*, **77**, 415.
Feinberg, S. M. (1946). *J. Amer. med. Ass.*, **132**, 702.
Frugoni, C., and Serafini, U. (1950). Rapports 2e. Congr. int. Asthme.
Gaddum, J. H. (1948). *British Medical Journal*, **1**, 867.
Hawkins, D. F., Mongar, J. L., and Schild, H. O. (1951). *J. Physiol.*, **113**, 26P.
Holtz, P. (1937). *Klin. Wschr.*, **16**, 1561.
Jiménez Díaz, C., Perianes, J., Arjona, E., Lorente, L., and Aguirre, M. (1950). *Bull. Inst. med. Res.*, **3**, 229.
Kapeller-Adler, R. (1949). *Biochem. J.*, **44**, 70.
—— (1951a). Ibid., **48**, 99.
—— (1951b). Ibid., **48**, xxi.
Katz, G., and Cohen, S. (1941). *J. Amer. med. Ass.*, **117**, 1782.
McHenry, E. W., and Gavin, G. (1931). *Trans. roy. Soc. Can.*, B, **25**, 101. Quoted from Rose and Browne (1938).
Marcou, I., Gingold, N., and Parhon, C. C., jun. (1937). *Bull. Acad. Méd. Roumanie*, **3**, 366.
Mongar, J. L., and Schild, H. O. (1951). *Nature, Lond.*, **167**, 232.
Roberts, M., and Adam, H. M. (1950). *Brit. J. Pharmacol.*, **5**, 526.
Rose, B. (1941). *J. Immunol.*, **42**, 161.
—— (1947). *Amer. J. Med.*, **3**, 545.
—— (1950). *Proc. First clin. A.C.T.H. Conf.*, 1949, p. 491. Blakiston Co., Toronto.
—— and Browne, J. S. L. (1938). *Amer. J. Physiol.*, **124**, 412.
—— Karady, S., and Browne, J. S. L. (1940). Ibid., **129**, 219.
Serafini, U. (1948). *J. Allergy*, **19**, 256.
Swanberg, H. (1950). *Acta physiol. scand.*, **23**, Suppl. 79.
Tabor, H., and Mosettig, E. (1949). *J. biol. Chem.*, **180**, 703.
Urbach, K. F. (1949). *Proc. Soc. exp. Biol., N.Y.*, **70**, 146.
Weiss, S., Robb, G. P., and Ellis, L. B. (1932). *Arch. intern. Med.*, **49**, 360.

The *Report of Proceedings* of the Scottish Society of the History of Medicine has just been published; membership now exceeds the hundred mark, and three meetings were held during the year—at Edinburgh, Glasgow, and Aberdeen. At the annual general meeting the president talked about Maya and Inca medicine. When the Spaniards invaded Southern and Central America they found that the Incas had a firmly established socialist state in Peru and Bolivia at a time when the Aztecs were committing genocide by mass sacrifices in Mexico; the Mayas, or Greeks of the New World as they have been called, were living in a remarkable state of civilization, sculptural remains of which may still be seen at Chichen Itza and elsewhere. Little is known of their system of medicine, though they made use of a wide range of medicinal plants, a practice which is now dying out as synthetic drugs become cheaper and easier to obtain; an interesting feature of the modern Maya is his low pulse rate—averaging 52 per minute. The main sources of the early medical history of the Incas are to be found in earthenware jars, some of which are decorated with designs representing diseases. The results of mutilation of the lips and nose, sacrificial and punitive, are also depicted, and also the operation of trephining—practised with the idea of allowing the demon of disease to escape from the victim's head. This operation was one of the early practices of the people of ancient Peru, and the spade-shaped knife used has been adopted as the emblem of the Peruvian Academy of Surgery. Another interesting practice prevalent among the Incas was the embalming of the dead. The corpse was flexed at all the joints in the foetal position, set in a basket, and treated with varnishes and resins; it was then wrapped in many layers of cloth and the resulting pear-shaped bundle placed in an artificial tomb.

SOME CONSIDERATIONS CONNECTED WITH THE CLASSIFICATION AND EXPLANATION OF NAEVI AND NAEVOID CONDITIONS*

BY

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The word "naevus" is the Latin for a "mole" or "birth-mark," but should, I think, now be used to signify a usually more or less localized congenital or developmental abnormality of tissue as evidenced by its form, bulk, texture, colour, and functional and metabolic activity—including urtication, pruritus, lipoid or amyloid or calcareous deposits, etc. This is the extended definition of "naevus" as I use the term.

Dermatologists are naturally more interested in superficial naevi, but it is obvious that internal parts may be analogously affected. In support of this one need only mention the Sturge–Kalischer–Weber disease, a developmental condition in which a vascular naevus, especially of the trigeminal region of the face, is associated with an ipsilateral vascular abnormality of the underlying leptomeninges, evidently of similar naevoid nature. Patches of peritoneal pigmentation and certain connective-tissue thickenings and minute fibrous (sometimes calcifying) nodules and adenomatous "tumours" in various viscera may also be mentioned here. I would include as naevoid the rare developmental disease known as "osteochondromatosis" of articular synovial membranes (cf. Lauber and Parkes Weber, 1950). But with few exceptions I shall put off for another occasion references to what I regard as internal and visceral naevi or naevoid conditions, including naevoid abnormalities of the blood cells.

A great difficulty experienced in dividing naevi into groups is that many of them, according to various methods or aspects of classification, are found to belong to more than one group. Local developmental deficiency or excess of epidermis, dermis, or subcutaneous tissue (and subcutaneous fat) and of local blood supply and lymphatics may explain some naevi, but "naevus anaemicus" (Voerner) may occasionally be associated with haemangiectatic naevus (cf. Weber and Harris, 1932; Weber, 1933; Wakeley and Weber, 1936). So, also, a pigmented naevus may, as is well known, be surrounded by an area of hypochromic or achromic skin. The first example I saw of this, rendered specially remarkable by the fact that the patient also had chronic obstructive jaundice, was shown by H. D. Rolleston (1910) before R. L. Sutton (1916) described his two cases of "leucoderma acquisitum centrifugum" (cf. Weber, 1924).

Atavistic Naevi.—Piebaldism is perhaps the most striking example. Some pigmented and hairy naevi may well have an atavistic or "simian" origin—for instance, the extensive hairy naevi of bathing-drawers localization. Many congenital cysts and sinuses are atavistic (branchiogenic, etc.)—that is to say, they are developed from remnants of structures which were normal in distant ancestors or at certain stages of human foetal life. An os penis in human beings has an atavistic explanation. Mongoloid pigmentary patches, especially over the lower sacral region, are perhaps to be regarded as atavistic, and so are the common pigment spots or papules representing supernumerary nipples.

Somewhat allied to atavistic naevi are the *organoid tumours*, the best-recognized example of which is the *glomus tumour* ("glomangioma"), which is a "hamartomatous" dysplasia of the glomus organ of Masson, sometimes occurring in situations where a normal glomus organ would not be expected.

Personally I regard Pringle's sebaceous adenomata as organoid tumours of sebaceous glands (cf. Weber, 1950a). As in glomus tumours the degree of vascularity may vary greatly, so in sebaceous adenomata the relative proportion of blood vessels and sebaceous cells may differ widely in different specimens.* The association of sebaceous adenomata with tuberous sclerosis of the brain is well known, but they (Pringle's sebaceous adenomata) may occur in apparently otherwise normal individuals—in fact, as the only sign of "epiloia." (A post-mortem examination after some fatal accident may nevertheless reveal the unexpected presence of tuberous sclerosis of the brain.) Fibrous naevi of the skin and naevi of abdominal viscera may also constitute a feature in epiloia.

Naevi as Local Non-progressive Variants of Generalized Diseases

Neurofibromatous Naevi.—Many otherwise normal individuals have one or two molluscous fibromata or one or two *café-au-lait* patches of cutaneous pigmentation. These I would term neurofibromatous naevi. There is a congenital or developmental naevoid type of *cutis verticis gyrata*, or "bulldog scalp," the microscopical structure of which is neurofibromatous. It deserves to be included as a neurofibromatous naevus (cf. Weber, 1950b). I shall return to this subject further on.

Naevi Due to Local Abnormalities of Intracellular Metabolism

Xanthomatous Naevi.—It seems to me that as xanthelasma palpebrarum may appear in young persons—sometimes in more than one individual in the same family—without ever leading to serious xanthomatous disease, it may well be regarded in such cases as a local naevoid condition, due to a local abnormality of intracellular cholesterol metabolism, which remains confined to the affected region and never involves other and more important parts of the body. (The spots in children which have been termed "xantho-naevo-endotheliomata" by J. E. R. McDonagh in 1912 should also be mentioned here.) Mr. Eugene Wolff (1951) thinks that xanthelasma palpebrarum is due to a lipoid change in the cells or in a down-growth from the cells which he regards as unicellular sebaceous glands in the basal layer of the epidermis at the inner part of the eyelids; in these altered cells he finds doubly refractile lipoid material. I do not think that this view—whether right or wrong—affects what I have said about the probable naevoid nature of xanthelasma palpebrarum in young persons, but I shall refer to this subject further on.

*Communicated to the Annual Meeting of the British Association of Dermatology, Oxford June 30, 1951.

*If I were asked whether I wished to include all glandular adenomata under the term "organoid tumours" I would reply: "No, only those in which the 'tumour' consists not only of the derivatives of the glandular cells but also of vascular and other non-glandular constituents of the gland in question." Thus, in the sebaceous adenomata of Pringle the non-glandular blood-vascular element may sometimes be the chief constituent, causing it to resemble a small haemangioma.

Calcinosis Naevi

Multiple calcifying lesions may be present in the skin and subcutaneous tissue of young children without involvement of other parts of the body or of the general health. In such a case (that of a little girl) one of the lesions was seen to be present at birth. Chronic calcareous discharge occurred from one or two of the lesions when the child was 2 years old, without any disturbance in her general development or health. It seems a legitimate suggestion that the lesions in question are due to a local abnormality of intracellular calcareous metabolism. For being permitted to see this unique case I am greatly indebted to Dr. G. B. Dowling. Though no biopsy was possible, I think one may practically exclude the diagnosis of calcifying epithelioma, which I regard as also naevoid in nature.

Primary local amyloid "tumours" (naevi) of the tongue, conjunctivae, nose, etc., and *primary generalized amyloidosis*, notably the cases with *amyloid macroglossia* (Lubarsch–Pick syndrome), should be mentioned here (cf. Weber, 1949).

Connexion Between Haemangiectatic Naevi and Associated Hypertrophy of Limbs or Neighbouring Tissue

What I called haemangiectatic hypertrophy of limbs in 1918 (Weber, 1918) is now fairly well known as a developmental naevoid condition (cf. Reichenheim, 1943), and it is certain that parts other than the extremities may be occasionally analogously affected. There is some justification in using the term "haemangiectasia hypertrophicans, Klippel–Trenauny–Parkes Weber" (see Ciarrocchi, 1950). In this class of cases are not rarely present developmental phlebarteriectasis and arteriovenous communications which I regard as themselves naevoid conditions. So-called "congenital varicose veins" are sometimes developmental conditions of the same naevoid nature.

In the various types of angiokeratosis (haemangiokeratosis) there seems to be a causal connexion between the epithelial overgrowth and the haemangiectatic basis. Angiokeratomata of the fingers are, I think, rarer than the multiple very small angiokeratomata of the scrotum (I have not heard of analogous angiokeratomata of the vulva), which constitute a condition similar to the very rare haemangiokeratomatosis (multiple angiokeratoma) involving the trunk and thighs. Allied to these cases are, I think, the various developmental conditions of patchy hyperkeratosis of the hands, feet, or other parts on an erythematous or telangiectatic basis.

Naevi and Age

It is still held by some that naevi must be present at birth or appear during the early years of life, but, according to my definition, this is not so. Naevi may first appear during middle life or during old age, as in so-called sebaceous naevi. There is occasionally a form of senile "degenerative" venous naevus of the tongue or lips in old persons.

I now believe that the condition described by Parkes Weber and Hellenschmied (1930) as "telangiectasia macularis eruptiva perstans" should be regarded as a form of naevus. The crops of spots appear especially (but not only) in obese middle-aged women, without any obvious cause, and persist. As this disease is intimately allied to, if not actually a telangiectatic variant of, *urticaria pigmentosa* with little pigmentation and little urtication, I regard urticaria pigmentosa also as a naevoid condition. In the naevoid group I feel likewise inclined to place "inborn urticaria factitia" and inborn dermographia (pruritus not necessarily present). Minute "pruriginous naevi" (spots of idiopathic pruritus), appearing in adult life, might constitute the bases on which by repeated scratching prurigo nodularis ultimately develops (cf. Elford, Weber, and Lowenberg, 1950).

Naevi and Mutation of Somatic Cells

I would of course agree that many of the developmental conditions referred to in this paper are, like numerous developmental abnormalities in the osseous and other systems, to be regarded as originally due to gene-mutation in germ cells; but I think also that there are acquired minor dermatological abnormalities, such as "ruby spots," which might be regarded as results of mutation in somatic cells, if it could be proved that such take place. *Ruby spots* (Campbell de Morgan's spots), though present in practically all adults (and some children), tend to be more numerous in elderly persons. I regard them as minute telangiectatic naevi which are possibly due to spontaneous mutation of somatic cells. Any adult who has not one or more ruby spots is a rare exception—in fact, in this respect abnormal (Weber, 1946). They are not to be confused with the rarer spider telangiectases—"stellate naevi"—which may be congenital, though they are often associated in some way with liver disease.

Spontaneous Disappearance or Partial Disappearance of Naevi

It is well known that, in children, capillary vascular naevi may after birth fade or partially or completely disappear spontaneously. "Ruby spots" and minute telangiectatic naevi may sometimes disappear (? by spontaneous thrombosis or atrophic closure of blood vessels). McDonagh's xanthonaevo-endotheliomata in children may spontaneously disappear. I have known one case in which slight but definite xanthelasma palpebrarum disappeared spontaneously. So-called mongoloid patches may disappear in early life. Some other naevi in elderly persons may, I think, diminish or necrose spontaneously.

Naevi and Malignant Neoplasms

The occasional supervention of malignant neoplasms on moles is well known ("naevocarcinoma"). Seborrhoeic naevi in elderly persons may occasionally become carcinomatous and malignant melanomata may develop from pigment naevi. In the rare familial recessive mendelian disease *xerodermia pigmentosa* (xeroderma pigmentosum) the skin is excessively sensitive to exposure to sunlight, which gives rise to warty lesions which ultimately become carcinomatous. Equally well known is the supervention of fatal malignant disease in cases of familial polyposis of the intestine (notably colon) which may be regarded as a familial intestinal naevoid condition (cf. Cockayne, 1927; Dukes, 1930; Lewis, 1941).

Here I would allude to the rare *syndrome of melanin spots (pigment naevi) on the lips and oral mucosa with intestinal polyposis which may lead to intussusception.* The first known examples were in twin sisters described by Sir Jonathan Hutchinson (1896) and J. T. Conner (1895). Afterwards by the kindness of Dr. Conner I

was able to examine one of the twins (Weber, 1919), but no evidence of intestinal polyposis was discovered till later. Jeghers, McKusick, and Katz (1949) collected their own and all known cases bearing on the subject in a paper entitled "Generalized Intestinal Polyposis and Melanin Spots of the Oral Mucosa, Lips and Digits: A Syndrome of Diagnostic Significance." An excellent example of this syndrome with gastric as well as jejunal polyposis was shown by N. C. Tanner (1951) at the Royal Society of Medicine (Clinical Section) on December 8, 1950. Similar familial pigment spots of the lips and mouth without known intestinal polyposis have been published from time to time. The complete syndrome may be regarded as a fifth kind of "phakomatosis" in J. van der Hoeve's use of the term (Weber, 1951)—see below.

Naevus and Naevoid Diseases and the "Phakomatoses" (Naevus Tumour Diseases) of van der Hoeve

J. van der Hoeve (1938) has grouped the four developmental diseases—Recklinghausen's neurofibromatosis, Bournville's disease (tuberous sclerosis, epiloia), the Lindau–Hippel disease, and the Sturge–Kalischer–Weber disease—as what he terms "phakomatoses." The Greek word φακός (lentil,* birth-mark) is medically equivalent to the Latin *naevus*. I think one must agree that van der Hoeve's phakomatoses are of naevoid nature. So what I have termed neurofibromatous naevi would be included under the heading "neurofibromatosis, a developmental naevoid disease." But if what I have termed "xanthomatous naevi" be regarded as minor localized and non-progressive forms of the developmental metabolic disease xanthomatosis, then xanthomatosis must be accepted as also "naevoid" in nature. This consideration would lead to the question: Are all "inborn errors of metabolism" (A. E. Garrod) to be regarded as naevoid in nature? I am not prepared to go so far, but obviously the whole difficulty is partly one of terminology. To assert that all inborn errors of metabolism are of naevoid nature would be like saying that all conditions resulting from gene abnormalities are of naevoid nature.

"Naevus" and "Naevoid"

In the present state of knowledge I think it is permissible to use the words "naevus" and "naevoid" (that is to say, like a naevus) synonymously. Instead of "naevoid," strictly speaking one should of course say "phakoid," using two Greek words instead of a Latin and a Greek word joined together. However, in this paper I have used the word "naevoid" in respect of conditions which are generally regarded as not naevus, but which I suggest are of naevus-like nature. I speak of a neurofibromatous "naevus," though I regard the whole disease, neurofibromatosis, as "naevoid"—that is, as van der Hoeve would say, a "phakomatosis." Similarly, I would speak of a Pringle's naevus; but the whole disease, epiloia, I would call a naevoid disease—that is, a phakomatosis (van der Hoeve). From my point of view, I would speak of diseases like *telangiectasia macularis eruptiva perstans* and *urticaria pigmentosa* and *inborn urticaria factitia* (which are not generally regarded as naevus conditions) as of naevoid nature. The Sturge–Kalischer–Weber disease or syndrome often presents a trigeminal vascular naevus as a striking feature, but many would object to call the whole syndrome a naevus condition, though I think it is obviously of naevoid nature, a phakomatosis of van der Hoeve.

*Phakos (lentil) is of course used also to mean the crystalline lens of the eye. When I first heard of "phakoma" (naevus "tumour") I was puzzled concerning what a tumour of the crystalline lens could be.

[Note.—A list was added of most of the external and some of the internal conditions which Dr. Weber would (often doubtfully) classify as naevi or naevoid, but there was not time to read it.]

References

Ciarrocchi, L. (1950). *Arch. ital. Derm.*, **23**, 197.
Cockayne, E. A. (1927). *Cancer Rev.*, **2**, 337.
Conner, J. T. (1895). *Lancet*, **2**, 1169.
Dukes, C. (1930). *Cancer Rev.*, **5**, 241.
Elford, W. P., Weber, F. P., and Lowenberg, M. (1950). *Proc. roy. Soc. Med.*, **43**, 835.
Hutchinson, J. (1896). *Arch. Surg., Lond.*, **7**, 290.
Jeghers, H., McKusick, V. A., and Katz, K. H. (1949). *New Engl. J. Med.*, **241**, 993, 1031.
Lauber, H. C., and Weber, F. P. (1950). *Med. Pr.*, **224**, 121.
Lewis, E. E. (1941). *Proc. roy. Soc. Med.*, **34**, 558.
Reichenheim, P. P. (1943). *St. Bart's Hosp. J.*, **4**, 53.
Rolleston, H. D. (1910). *Proc. roy. Soc., Med.*, **3**, Clin. Sect., 195.
Sutton, R. L. (1916). *J. cutan. Dis.*, **34**, 797.
Tanner, N. C. (1951). *Proc. roy. Soc. Med.*, **44**, 405.
van der Hoeve, J. (1938). *Nederl. Tijdschr. Geneesk.*, **82**, 4418.
Wakeley, C. P. G., and Weber, F. P. (1936). *Int. Clin.*, **1**, 145
Weber, F. P. (1918). *Brit. J. Child. Dis.*, **15**, 13.
—— (1919). *Quart. J. Med.*, **12**, 404.
—— (1924). *Brit. J. Child. Dis.*, **21**, 202.
—— (1933). *Proc. roy. Soc. Med.*, **36**, 126.
—— (1946). *Rare Diseases and Some Debatable Subjects*, p. 51. Staples, London.
—— (1949). *Further Rare Diseases and Debatable Subjects*, p. 52. Staples, London.
—— 1950a). *Med. Pr.*, **223**, 513.
—— 1950b). *Proc. roy. Soc. Med.*, **43**, 556.
—— (1951). *Med. Pr.*, **225**, 658.
—— and Harris, K. E (1932). *Brit. J. Derm.*, **44**, 77.
—— and Hellenschmied, R. (1930). Ibid., **42**, 374.
Wolff, E. (1951). *Lancet*, **1**, 188.

AN EXPLANATION OF THE "PRIMARY ATYPICAL PNEUMONIA" SYNDROME

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In the course of the past two years we have seen over 500 cases of a condition which we believe to be an aspiration pneumonia, the pulmonary lesions of which are confined to certain local regions of the lung. This, both clinically and radiologically, is similar to descriptions of primary atypical pneumonia and to many of the so-called virus pneumonias. We wish to dispel much of the mysticism associated with this group of conditions and to destroy the concept of atypical pneumonia as at present described.

The features of our own cases are described; the reported features of primary atypical pneumonia are reviewed, and the two are compared. Reasons are given for our attack on the present conception of atypical pneumonia, and the significance of the altered point of view is discussed.

Present Series

Material.—The cases have been drawn from young men who had already been passed by a medical board and who were undergoing the first few weeks of initial

basic military training in recruit training camps. Nearly all were radiologically normal on entry, but a small number were picked up by the mass miniature radiography examination. Large numbers of young men are for the first time concentrated in such training camps; each week there are repeated intakes from all parts of the country, and at the same time comparable numbers of trained men are posted to other units. Upper respiratory infections are common in such an environment, and the pulmonary lesions to be described followed such infections. Similar cases are often seen in civilian radiological practice but are not included in this series.

Clinical Features

There was no constant clinical picture, as the illness varied greatly in intensity and duration. Most patients were moderately ill for the first 24 to 48 hours, and, though some were seriously ill, none died. Most were febrile and felt miserable, their discomfort being aggravated by troublesome pain and cough. In some the illness was slight and would not normally entail absence from work.

A few days after the onset of an upper respiratory infection one or more of the cardinal signs of pulmonary disease developed.

Cough was invariable, often of a characteristically harsh and repetitive nature. In a small number of patients stress fractures of the ribs were detected.

Sputum was usually absent or scanty in the early stages but was almost invariably present later in the course of the illness. In many instances this was yellowish green in colour and obviously purulent. *Blood-staining*, though often unnoticed by the patient, was a frequent finding.

Chest pain was often present and in many instances was pleural in type. In others it consisted of an ache or discomfort, or an awareness of "something wrong in the chest." Characteristic pleural pain was most common in association with anterior pulmonary lesions, while those with involvement of the lower lobes experienced either referred pain in the shoulders or abdomen, or complained of backache. The site of the chest pain was frequently of assistance in locating the lesion, though rarely the pain was referred in the first instance to the opposite side.

Dyspnoea was seldom noted and certainly could not be regarded as a characteristic feature. Significant loss of weight did not occur.

Fever was in many cases quite high initially, but in the majority had subsided within a few days. It was common for there to be several days of low-grade pyrexia before the temperature finally settled. Occasionally there was a second rise in temperature.

The frequency of these clinical features was as follows:

Cough	100%
Sputum (initially)	78%
Sputum (subsequently)	practically 100%
Blood-staining of sputum (noted)	18%
Chest pain	58%
Referred pain	9%
Dyspnoea	1%

Signs

There was always an upper respiratory tract infection either at its height or in the decline. This usually consisted of coryza, nasopharyngitis, tonsillitis, or sinusitis and requires no further description.

Physical examination did not usually reveal any generalized chest disease but sometimes signs suggesting a general bronchitis were found. Such generalized signs tended to mask the presence of local abnormality.

Local chest signs consisted of added sounds in the form of crepitations and coarse moist sounds, together with diminished air entry and impaired percussion note over the site of the pulmonary disease. Such signs were often strictly localized to small areas of the chest wall and in general they were difficult to elicit and could not be relied upon. Further, they bore little relation to the extent of the pulmonary disease revealed by radiography.

Course

It was not easy to estimate the duration of the illness on clinical grounds alone. The initial cold or nasopharyngitis ran its customary short course. Recovery from the general illness was usual within a few days though productive cough and chest pain and the radiological changes sometimes persisted for several weeks. The effect of sulphonamides and penicillin on the clinical course was difficult to interpret; even in those cases in which there was some evidence of response little corresponding radiological improvement followed.

Clinical Pathology

Laboratory examinations were restricted to examinations of the sputum and the blood. In most cases the sputum was examined repeatedly by direct means for tubercle bacilli, with negative results. On culture there was usually a heavy growth of those organisms normally found in the upper respiratory tract. Occasionally a predominant organism such as *Streptococcus viridans* was found. Detailed bacteriological study of each case was not undertaken.

The total white-cell count was not as a rule significantly raised, the usual range being from 7,000 to 14,000 per c.mm. Rarely counts of up to 20,000 per c.mm. were found, when the rise was mainly due to a polymorphonuclear leucocytosis.

The erythrocyte sedimentation rate was occasionally estimated and was usually found to be raised, sometimes considerably.

Radiology

The one constant feature of all cases was the anatomical localization of the disease to bronchopulmonary segments or subsegments, so that the appearances depended on the portions of lung involved. In order to define the site and extent of the lesions, and in some instances to see certain retrocardiac and basal lesions at all, it was found essential to have lateral films in every case.

Every degree of abnormality was seen, from dense "ground-glass" opacity to increased density of the bronchovascular markings. Some degree of collapse within the lesion was very frequent, but occasionally this could be detected only by most careful inspection of the films. Some shift in the position of the interlobar fissures and crowding of the broncho-vascular pattern were in most instances the only signs of collapse present. Here, again, the lateral projection was found to be essential because, as one would expect, such local lesions rarely produced gross signs of collapse. Lesions were generally confined to the basal segments of either or both lower lobes, to the lower division of the lingula of the left upper lobe, or to the anteromedial portion of the

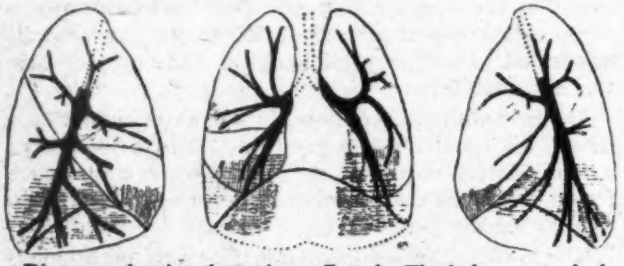
right middle lobe. Occasionally lesions in the axillary divisions of the subapical or the pectoral segments of the upper lobe were seen, but these were usually associated with involvement of other sites. Such broncho-pulmonary radiological changes are not of course specific for this condition, because they can be reproduced by any cause of segmental de-aeration.

Enlargement of the hilar glands was rarely noted and in no case appeared to cause bronchial compression. Occasionally glandular enlargement developed subsequent to an infected segmental lesion. *Pleural effusion* was seldom encountered and was always small and quick to resolve. *Abscess formation* within the lesion was encountered twice. On both occasions the cavity was small and was situated in an axillary subsegment of an upper lobe; each rapidly and spontaneously resolved.

The table and diagrams show the distribution and incidence of the lesions in our series of cases.

Distribution and Incidence of Lesions

Isolated lesions:	
Left upper lobe (excluding lingula)	0·5%
Lingula	5·4%
Left lower lobe	29·6%
Right upper lobe	1·4%
Right middle lobe	10·1%
Right lower lobe	23·1%
Combined unilateral lesions:	
Right middle lobe and others	9·1%
Lingula and others	5·7%
Combined bilateral lesions:	
Right middle lobe and others	1·4%
Lingula and others	2·5%
Right upper lobe and others	1·1%
Right and left lower lobes	10·1%
Total:	
Lower lobes	62·8%
Middle lobe and lingula	34·2%
Upper lobes (excluding lingula)	3·0%



Diagrams showing the regions affected. The lesions are principally in dependent broncho-pulmonary segments; a proportion of these lesions is obscured by cardiac and diaphragmatic shadows on the standard postero-anterior projection.

"Primary Atypical Pneumonia"

Definition.—"Primary atypical pneumonia" has been defined by Drew *et al.* (1943) and by Stephens (1948) as a term covering those respiratory illnesses with pulmonary radiological change for which no causal bacterium, virus, or rickettsia is known. Stuart-Harris (1950) describes the condition as a syndrome of respiratory tract infection characterized by varying symptoms, by radiological changes of particular character, and by lack of response to the sulphonamides or to penicillin.

Occurrence.—The disease has been described from all parts of the world, but principally from military sources. Large series have been reported from the United States Forces (Bowen, 1935; Campbell *et al.*, 1943; Dingle *et al.*, 1944; Owen, 1944), from the British Army (Drew *et al.*, 1943), and from the Royal Air Force (Kennedy, 1943). Other series have been reported from hospital staffs (Reimann and Havens, 1940; Kornblum and Reimann, 1940; Longcope, 1940) and from schools (Gill, 1938; Daniels, 1942). Most authors agree that there is a seasonal incidence, this being maximal in the winter and early spring.

Spread.—No clear evidence of the method of spread has been presented, though it has generally been considered to occur by droplet infection.

Incubation Period.—This has been stated to be between two and three and a half weeks by Kneeland and Smetana (1940), and between 7 and 21 days by Daniels (1942). Several authors describing series from military training centres have noted that most of their cases occurred within two to three weeks of first arrival at the unit (Langmuir, 1944; Dingle *et al.*, 1944).

Clinical Features

Campbell *et al.* (1943) give an excellent clinical description of a series of cases of atypical pneumonia. The onset of the disease is generally similar to that of an upper respiratory infection (Reimann and Havens, 1940).

The presence of *cough* is universally reported, and several authors note that it is sometimes of a peculiar hacking character, which causes distress to the patient and to his neighbours. Harvey (1944) reports 19 instances of rib fracture due to the cough.

Most authors describe the *sputum* as being scanty and mucoid initially but becoming more profuse and purulent. *Blood-staining* is commonly reported, and frank haemoptysis occasionally occurs.

Chest pain is usually situated in the site of the pulmonary lesion (Stephens, 1948) and it is described as often not truly pleural in nature but rather as a dull ache or discomfort. Drew *et al.* (1943) report the occurrence of pain elsewhere probably referred from the chest.

Fever is commonly reported to be quite high at the outset and this may persist for periods of two to seven days; resolution by lysis is the rule. In the more severe cases reported by Kneeland and Smetana (1940) the pyrexia was remittent and lasted for several weeks. Many authors, including Longcope (1940), describe what is termed a "biphasic pyrexia."

Signs

The clinical picture is reported as varying widely between slight illness and severe prostration in the rare serious cases.

Dyspnoea and cyanosis are uncommon, though they are reported in the most severe cases; the pulse rate is not usually much raised.

Physical signs in the chest are often absent or scanty initially, and are often strikingly so in relation to the pulmonary radiological change (Turner, 1945). Allen (1936) and Karpel *et al.* (1945) consider that as the physical signs are so sparse the diagnosis of atypical pneumonia rests on the radiological findings.

Course

Finland and Dingle (1942) state that in mild cases the illness may last for a period of about a week, while the more severe cases may be ill for six to eight weeks. In 851 patients reviewed by Wyman (1948) the average time taken for radiological changes to clear was 15.2 days. The average time spent in hospital in the cases reviewed by Drew *et al.* (1943) was 33 days. Before the advent of "aureomycin" no form of treatment was said to influence the course of the disease; recovery was usual and very few fatal cases have been recorded.

Clinical Pathology

The white-cell count is reported by almost all authors to be within the normal limits or only slightly raised.

Counts of over 15,000 cells are rare (Dingle *et al.*, 1944). The differential count is usually normal.

Culture of the sputum characteristically reveals only the common bacterial flora of the upper respiratory tract.

The cold-agglutination phenomenon has been associated with "primary atypical pneumonia" and it has often been referred to as a diagnostic aid. Scadding (1948), however, points out that the phenomenon appears to be non-specific, while Rich *et al.* (1945) state that it is found in many other conditions not related to atypical pneumonia. Bedson (1950) warns against acceptance of a rising titre of cold agglutinins as conclusive evidence of a specific infection.

Radiology

Most radiological descriptions of this condition are rather vague in detail, though that by Crysler (1946) is an exception. Various authors have described the lesion as consisting of fan-like shadows arising from the hilum and spreading out to the periphery. They are usually well localized though not sharply defined and are stated to be mainly in the "lower or middle zones." "Upper-zone" shadows have been described and so-called migrating lesions involving other pulmonary zones are not infrequent.

Many radiographs (Longcope, 1940; Dingle *et al.*, 1944) showing lesions apparently segmental in type have been reproduced, but cannot be confirmed as such in the absence of lateral projections. However, Drew *et al.* (1943) and Kennedy (1943) point out that the lesions are generally confined to a segment.

The presence of collapse within the lesion has been recognized by several authors (Campbell *et al.*, 1943; Kay, 1945). In the work of others, lack of lateral projections may have handicapped this recognition.

Comparison

It is evident from comparison of the features of "primary atypical pneumonia" with those of our own cases that no significant difference can be found. The illnesses occurred under similar circumstances and followed similar clinical courses. Radiologically the lesions are apparently identical and the results of laboratory investigations are essentially similar.

Aetiology

The view has been widely held that "primary atypical pneumonia" is an infective condition caused by an unknown virus. Detailed studies of the condition were made by Dingle *et al.* (1944), who stated in their conclusion: "It seems most likely that a new agent, probably a virus, is responsible for atypical pneumonia." Bedson (1950) stated that in those cases not caused by a known infective agent there was good evidence that they were of virus aetiology.

This view seems to have arisen largely because no other aetiological factor could be found. The low white count, the lack of response to chemotherapy, and the clinical resemblance to influenza-like illnesses have all contributed to this assumption. Furthermore, most cases were described from apparent epidemic outbreaks. Dingle *et al.* (1944), however, noted in their series that the characteristics of the outbreaks were not similar to those of known infectious diseases.

We believe that the cases we describe, together with most of the so-called atypical pneumonias, are in fact due to aspiration of products from the associated upper respiratory infections. Ramsay and Scadding (1939) held a similar view of a series of cases which appear to resemble the syndrome of "primary atypical pneumonia." The following points are put forward in favour of this concept:

1. The cases followed some upper respiratory infection. This infection was usually a nasopharyngitis or common cold, but similar lesions followed such other conditions as tonsillitis, sinusitis, tracheo-bronchitis, and true influenza.

2. All lesions occurred in dependent broncho-pulmonary segments or subsegments.

3. Symptoms often first arose when severe physical exercise had been undertaken in the presence of an upper respiratory infection; this is considered to be of great significance from three points of view: (*a*) Aspiration will more readily occur under conditions of rapid and gasping respiration, when the nasal passages are blocked and mucopus is present in the posterior nasopharynx. (*b*) Such patients were naturally ambulant at the time and therefore lesions occurred most frequently in the lower lobes. (*c*) It offers some explanation for the high attack rate amongst new recruits undergoing their initial training, whilst permanent administrative staff not undertaking such activity were very rarely affected.

4. Occasionally pulmonary lesions developed in patients already in hospital with upper respiratory infection. A group of five right middle lobe cases were all noted to occur in patients who usually sat or lay leaning towards the right side in order to observe the entrance to the ward. Radiological changes indistinguishable from those of primary atypical pneumonia have been seen in the surgical wards and would normally be termed post-operative aspiration pneumonias. In two instances in which lesions followed dental extraction with prolonged haemorrhage no upper respiratory infection was present.

These points appear to emphasize the unlikelihood of a pneumotropic virus being the cause of "primary atypical pneumonia." Why should a virus select isolated dependent broncho-pulmonary segments or subsegments? Why should a virus produce a segmental collapse? Why should a virus be suspected when identical lesions can follow aspiration of blood or other non-septic material? Why should it be possible to watch spread from a basal segment to the opposite upper lobe; the so-called migrating pneumonia? A similar "migration" of lipiodol after unilateral bronchography may often be observed. Why should there be no evidence of an acquired immunity? Recurrence in the same or in other segments has frequently been seen; such recurrence of a virus disease would be uncommon. Why should a specific pneumotropic virus produce such great variation in clinical course and degree of illness? The aspiration mechanism offers an explanation of this variation, as it is evident that the material aspirated may range from non-infected mucus to grossly infected pus.

Significance of this Point of View

The acceptance of an aspiration basis for "primary atypical pneumonia" greatly simplifies the understanding of the condition. It provides an explanation for its apparently obscure epidemiology, showing that its infectivity and method of spread are merely those of the upper respiratory infection. It shows that such pulmonary lesions are not fundamentally different from the pulmonary complications of childhood infections such as pertussis (Lees, 1950). It indicates that the condition will not be restricted to military sources; indeed, we have seen many cases among civilian patients both

in adults and in children, but these have not been included in the present survey. It offers a pointer to useful therapeutic measures to be adopted and we have extensively used such measures in the treatment of our cases.

Recognition of such radiological change as an aspiration segmental lesion has led us to perform further detailed investigations, and in this connexion over 200 cases have been examined by bronchography in order to study the changes in local bronchial pattern at the time of illness. The wide range of bronchial abnormality which may occur, some of which may be serious and irreversible, draws attention to the need for careful supervision and treatment of the original illness. These findings also contradict the usual view that "primary atypical pneumonia" is an essentially benign condition which resolves without serious sequelae.

This latter section of our work will form the subject of a separate publication.

Treatment

In the past no therapeutic measures were described as influencing the course of a "primary atypical pneumonia." More recently chloramphenicol and aureomycin have been widely advocated (Meiklejohn and Shragg, 1949).

When the aspiration basis for the lesions is appreciated it becomes evident that more simple measures may assist in the resolution of the pulmonary disease. Thus percussion postural drainage has been extensively used and has frequently assisted in the re-aeration and drainage of an infected segment. On occasion additional agents such as steam inhalations and short-wave diathermy have been employed.

The widely varying bacterial flora of such aspiration lesions gives some explanation for the varying response to chemotherapy and penicillin. Chloramphenicol and aureomycin can be regarded only as of use in those cases in which there is a considerable infective element due to organisms insensitive to penicillin. Their indiscriminate use as agents to combat the "virus of atypical pneumonia" must be regarded as unjustified; in any case no antibiotic can have significant effect upon the mechanical element of such segmental lesions.

Summary and Conclusion

The general features of a condition believed to be segmental aspiration pneumonia are described and a review of previous descriptions of primary atypical pneumonia is given. Comparison of the two conditions reveals no significant difference between them.

Reasons are given for doubting the viral origin of the pulmonary lesions. It is considered that they result from aspiration of products from an associated upper respiratory tract infection.

The significance of such a point of view is discussed and mention is made of possible complications and treatment.

Our experiences with this series of cases has led us to believe that the name and diagnosis "primary atypical pneumonia" is meaningless, as it is not a specific condition but merely represents a segmental aspiration pneumonia.

Without the co-operation of the medical authorities of the Royal Air Force and, in particular, Group Captain Rumball, the consultant in medicine, this work would not have been possible. We are grateful to the Director-General for permission to publish our findings. Dr. Robert Coope and Dr. P. H. Whitaker, whose clinical assistants we are, have given us every encouragement and placed the full facilities of their departments at our disposal. We are also grateful for much material assistance from the University of Liverpool.

References

Allen, W. H. (1936). *Ann. intern. Med.*, **10**, 441.
Bedson, S. P. (1950). *British Medical Journal*, **2**, 283.
Bowen, A. (1935). *Amer. J. Roentgenol.*, **34**, 168.
Campbell, T. A., Strong, P. S., Grier, G. S., and Lutz, R. J. (1943). *J. Amer. med. Ass.*, **122**, 723.
Crysler, W. E. (1946). *Amer. J. Roentgenol.*, **56**, 324.
Daniels, W. B. (1942) *Amer. J. med. Sci.*, **263**, 363.
Dingle, J. H., *et al.* (1944). *Amer. J. Hyg.*, **39**, 67, 197, 269.
Drew, W. R. M., Samuel, E., and Ball, M. (1943). *Lancet*, **1**, 761
Finland, M. and Dingle, J. H. (1942). *New Engl. J. Med.*, **227**, 342.
Gill, A. M. (1938). *British Medical Journal*, **1**, 504.
Harvey, R. M. (1944). *Amer. J. Roentgenol.*, **52**, 487.
Karpel, S., Waggoner, I. M., and McCown, O. S., jun. (1945) *Ann. intern. Med.*, **22**, 408.
Kay, E. B. (1945). *Arch. intern. Med.*, **75**, 89.
Kennedy, J. A. (1943). *Lancet*, **1**, 769.
Kneeland, Y., jun., and Smetana, H. F. (1940). *Bull. Johns Hopk. Hosp.*, **67**, 229.
Kornblum, K., and Reimann, H. A. (1940). *Amer. J. Roentgenol.*, **44**, 333.
Langmuir, A. D. (1944). *Amer. J. publ. Hlth*, **34**, 335.
Lees, A. W. (1950). *British Medical Journal*, **2**, 1138.
Longcope, W. T. (1940). *Bull. Johns Hopk. Hosp.*, **67**, 268.
Meiklejohn, G., and Shragg, R. I. (1949). *J. Amer. med. Ass.*, **140**, 391.
Owen, C. A. (1944). *Arch. intern. Med.*, **73**, 217.
Ramsay, H., and Scadding, J. G. (1939). *Quart. J. Med.*, **8**, 79
Reimann, H. A., and Havens, W. P. (1940). *Arch. intern. Med.*, **65**, 138.
Rich, C. (1945). *Canad. med. Ass. J.*, **53**, 265.
Scadding, J. G. (1948). *Lancet*, **1**, 89.
Stephens, J. W. (1948). Ibid., **1**, 703.
Stuart-Harris, C. H. (1950). *British Medical Journal*, **2**, 282.
Turner, W. D. (1945). *Lancet*, **1**, 493.
Wyman, A. C. (1948). *Dis. Chest.*, **14**, 568.

SERUM POTASSIUM DEFICIENCY DURING TREATMENT WITH SODIUM P.A.S. AND LIQUORICE EXTRACT

BY

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Cayley (1950) reported the occurrence of serum potassium deficiency in the course of treatment of three patients with pulmonary tuberculosis using *p*-aminosalicylic acid (P.A.S.). Heard, Campbell, Hurley, and Ferguson (1950) found evidence of this complication in 12 patients undergoing treatment with the drug.

Two patients with pulmonary tuberculosis have recently shown marked myasthenia while being treated with sodium P.A.S., and in view of the apparent rarity of the complication, judging from its absence in the numerous reports of the use of the drug, an account of it may be of interest. The implications of the metabolic changes found are examined.

Case 1

A girl aged 18 suffering from a breaking-down primary tuberculous lesion in the left upper lobe was receiving streptomycin, 0.5 g. twice daily intramuscularly, and sodium P.A.S., 4 g. five times daily by mouth, each dose containing 20 min. (1.2 ml.) of ext. glycyrrhiz. liq. *B.P.* as a flavouring agent. After 11 days' treatment and for the succeeding five days she suffered from intermittent pyrexia. She had previously been afebrile.

The tonsils showed a follicular exudate; the right tonsillar gland was found to be enlarged, and an erythematous rash appeared over the shoulders. Treatment was continued, and these signs disappeared. By the thirtieth day of treatment she complained of generalized stiffness in all limbs and of weakness and cramping pains in her legs. She remained

afebrile; her pulse rate was 80 and blood pressure 120/80. She did not appear to be overbreathing. There was marked weakness of all muscles of the neck, trunk, and limbs. Tendon reflexes were weak but could all be elicited, plantar reflexes were flexor, and no abnormality of sensation was found. Trousseau's sign was positive after 40 seconds' application of the inflated sphygmomanometer cuff, but, by contrast, Chvostek's sign was never elicited. Examination of several specimens of urine with Sulkowitch's reagent gave a normal reaction for calcium with a moderate precipitate. The serum calcium content was 8.8 mg. per 100 ml. and CO_2 combining power 85 vols.%.

Immediately after removing blood for examination she was given 10 ml. of 10% calcium gluconate, and a few minutes later Trousseau's sign was still found to be positive after three minutes. In spite of stopping sodium P.A.S. and giving oral ammonium chloride and further intravenous calcium gluconate, the muscular weakness and Trousseau's sign persisted, though becoming less marked, for 10 days. On the ninth day after onset of the weakness the serum calcium was 9.2 mg. per 100 ml., serum potassium 15 mg., and CO_2 combining power 62 vols.%. No cardiac abnormality was noted throughout, and for this reason, and because the possibility of a serum potassium deficit was not recognized until late, no electrocardiogram was made. Streptomycin was given throughout this complication and subsequently, with continued satisfactory progress.

Meanwhile Cayley's (1950) paper had appeared, and, while the changes he described might have accounted for the muscular weakness, it was not clear why such a marked Trousseau's sign had been found in our patient. The incident, however, led to fuller consideration of similar findings in another patient.

Case 2

An ex-miner aged 54 was admitted to hospital on May 12, 1950. He was known to have had pulmonary tuberculosis with tuberculous laryngitis for at least three years; and in November, 1949, he had had one testis removed for tuberculosis. He had not been treated at any time with streptomycin or P.A.S. For two months before admission he had complained of headache, particularly in the morning, that he staggered to the left on attempting to walk, and that when he tried to read "the lines ran into each other." He had noticed a sensation of "pins and needles" in the tip of his tongue and nose as well as round his mouth for about one month. His appetite had recently been poor, and he vomited from time to time.

Examination showed optic atrophy on the right due to a fractured skull 16 years previously. Anosmia was complete and taste was absent except for quinine. There was a right sixth-nerve palsy due to the old head injury. Nystagmus, maximal on looking to the left, was present, and there was slight past-pointing with the left arm, but no intention tremor or "rebound." Rombergism was not present, but on attempting to walk he staggered to the left. No other abnormality was found in the C.N.S. Cerebrospinal fluid pressure was 50 mm.; the fluid was clear and contained 42 lymphocytes per c.mm. The protein content was 80 mg., chlorides 744 mg., and sugar 64 mg. per 100 ml. The Wassermann reaction was negative (also in blood). Tubercle bacilli were not found on direct examination or on animal inoculation. The erythrocyte sedimentation rate (Westergren) was 22 mm. in the first hour. On admission the urine was acid, specific gravity 1027, and contained some albumin and pus cells. Tubercle bacilli were subsequently isolated by culture from a 24-hour specimen of urine. The albuminuria cleared up soon after admission, and was found later only when haematuria was occurring. A diagnosis of disseminated tuberculosis with cerebellar involvement was made and treatment with streptomycin, 0.5 g. twice daily intramuscularly, and sodium P.A.S., 3 g. six times daily, was begun on May 22. The P.A.S. was given in a mixture containing 20 min. (1.2 ml.) of ext. glycyrrhiz. liq. *B.P.* per dose as a flavouring agent. He had been vomiting intermittently since admission, and during the first few days of treatment lost several doses of P.A.S. in this way; no further vomiting occurred after June 5, and sodium P.A.S., 3 g. five times daily, was continued.

On June 29 he complained of numbness of the thumb and index and middle fingers of the left hand, but no objective changes were found. Tendon reflexes were all present. On July 12 he complained of stiffness and weakness in both arms, so P.A.S. therapy was stopped, but the streptomycin injections were continued.

On July 13 he was very weak and unable to sit up or feed himself; he had no difficulty in respiration or swallowing, and, objectively, power in muscles of cranial innervation, as in the legs, was good compared with that in the arms. Reflexes in the arms were weak; only the right upper abdominal reflex could be elicited, but those in the legs appeared normal. Trousseau's sign was present after two minutes' compression, but Chvostek's sign remained absent throughout. The only sensory abnormality found was depression of pain sensibility over the tips of the fingers of the left hand. The pulse rate was 84, and no abnormality was found in the cardiovascular system except that the blood pressure was slightly raised to 150/100.

As the condition showed some superficial resemblance to myasthenia gravis the patient was given 1 mg. of neostigmine hydrobromide with atropine sulphate, 1/100 gr. (0.65 mg.) intramuscularly, without any apparent effect. The serum potassium was found to be 8.5 mg. per 100 ml. (duplicate estimations). Subsequent changes in the serum potassium concentration are shown in Table I.

TABLE I.—*Serum Electrolyte and CO_2 Changes*

Date	Weight		Potassium mg./100 ml.	Calcium mg./100 ml.	Sodium mg./100 ml.	CO_2 Comb. Power Vols.%	Chlorides (as NaCl) mg./per 100 ml.
	lb.	kg.					
15/6/50			18·0				
17/6/50	116	52·6					
1/7/50	117	53·0					
8/7/50	116	52·6					
13/7/50			8·5	10·0			
15/7/50	114	51·7	7·6		323	88	454
17/7/50			8·1		324	97	
20/7/50			10·7		336	63	
21/7/50			8·1				
24/7/50			7·6			79	
25/7/50					333	75	
28/7/50			10·4			82	
29/7/50	111	50·3	15·8	9·2		78	
31/7/50			22·1			79	
2/8/50			21·8			73	
3/8/50				10·5			
6/8/50	106	48·1					

On July 14 he developed marked haematuria. This persisted for several days, and was thought to be due to renal tuberculosis, as tubercle bacilli had been identified in his urine on June 9. The haemorrhage may have been precipitated by hypoprothrombinaemia, as this constantly follows the administration of P.A.S.

On July 15, in view of the persistent Trousseau's sign and raised CO_2 combining power, he was given ammonium chloride, 1 g. two-hourly by mouth during waking hours. This was continued until August 6.

On July 19 he developed prolapse of the rectum, probably due to weakness of the muscles of the pelvic floor. At this time he could raise his hands to feed himself, though power and reflexes in the legs were weaker than previously. From July 26 to August 1 he was given potassium chloride, 3 g. four times daily by mouth. On July 31, when the serum potassium had risen to 22.1 mg. per 100 ml., power in all limbs was much improved, reflexes were more readily elicited, and Trousseau's sign was positive only after four minutes' compression. Within a further two days the myasthenia had entirely disappeared, though the paraesthesiae in the left hand persisted without objective sensory

changes. Throughout the incident muscle and reflex weakness had been more marked in the arms and trunk than in the legs, whereas muscles of cranial innervation were conspicuously unaffected.

Electrical reactions in the right quadriceps and right forearm flexor groups of muscles were examined almost daily from July 22 to August 15, using a Ritchie-Sneath stimulator. The results are summarized in Table II. The

TABLE II.—*Muscle Electrical Thesholds*

Muscle Group:	Right Quadriceps				Right Forearm Flexor			
Pulse length (millisecs.)	100	10	1	0·1	100	10	1	0·1
Hypokalaemic phase:								
Mean threshold voltage	34·6	35	49·4	51·6	26·75	28·0	43·0	45·0
Range of threshold voltage	32–7	32–8	40–64	42–64	22–30	22–30	35–50	35–50
No. of observations	5				4			
Standard deviation	2·55	3·0	10·85	10·74	4·02	4·02	6·28	7·08
After recovery:								
Mean threshold voltage	30·5	30·7	41·3	43·3	26·5	26·5	35·2	36·1
Range of threshold voltage	28–35	30–5	35–48	36–48	22–8	22–8	25–42	25–48
No. of observations	10							
Standard deviation	1·84	1·63	4·68	3·68	2·54	2·54	5·55	6·72
Difference of means	4·1	4·3	8·1	8·3	0·25	1·50	7·8	8·9
Standard error of difference	1·28	1·43	5·1	4·94	2·22	2·22	3·2	3·6

In the case of the quadriceps, when the pulses were of 100 and 10 m.secs. duration the observed differences were more than three times their standard error, whereas with pulses of 1 and 0·1 m.sec. the differences were less than twice their standard error For the forearm flexor group the reverse is true, and only with the shorter pulses of 1 and 0·1 m.sec. were the differences significant (2·4 times their standard error).

voltage required to elicit a contraction at a given pulse length, frequency remaining constant at approximately five per second, is expressed as the mean of daily observations made, first, when the muscle weakness was present, and subsequently when muscle power was normal.

It will be seen that after muscle power returned to normal the voltage required to elicit a contraction at all pulse lengths examined was diminished, and, further, that in the thigh muscles the difference was more striking with the longer pulses, and in the arm with the shorter pulses. This may be an expression of the different behaviour of muscles in various parts of the body as a result of potassium deficiency, which was evident on clinical examination and which is shown to be capable of measurement.

The patient's condition in December, 1950, was satisfactory in that he showed none of the earlier evidence of cerebellar disorder, he had put on weight, and tuberculous activity elsewhere was apparently in remission.

Discussion

In Case 1 the markedly positive Trousseau's sign with the complaint of stiffness and cramps led to the conclusion that the weakness was the result of tetany, though the absence of Chvostek's sign and the normal urinary excretion of calcium raised doubts about this. The serum calcium, however, was found to be in the lower range of normal (8.8 mg. per 100 ml.); this is above the usual renal threshold for calcium, and is in accord with the positive Sulkowitch reaction in the urine. The high CO_2 combining power (85 vols.%), together with the slightly lowered serum calcium, was thought to account for the presence of Trousseau's sign, and only when this sign and the muscle weakness failed to respond to the administration of ammonium chloride and calcium gluconate was the possibility of potassium deficiency considered. By this time the serum potassium was 15 mg. per 100 ml.

The experience with Case 1 led to early estimation of serum potassium in Case 2, and an E.C.G. (see Fig.) was recorded (June 6) sixteen days after starting sodium P.A.S. therapy. It will be noted that this was already abnormal in form. Once more the onset of weakness with paraesthesiae in the fingers suggested tetany, and Trousseau's sign was found positive, though again Chvostek's sign remained absent throughout. These signs persisted until the serum potassium returned to normal after the administration of potassium chloride.

It seems clear that the muscle weakness was related to the low serum potassium, as in the second patient both findings were corrected simultaneously by giving potassium chloride. Why this potassium deficit should have occurred with the administration of sodium P.A.S. in these two patients while it has not been observed in others is difficult to explain. Borst *et al.* (1950) described a liquorice extract with deoxycortone-like action. This in retrospect seemed to offer a possible explanation, as both of the patients reported had been taking sodium P.A.S. in a mixture containing 20 min. (1.2 ml.) of ext. glycyrrhiz. liq. *B.P.* per dose; and Cayley (1950, personal communication) has stated that his three patients had all had liquorice with their P.A.S. In some respects the metabolic changes induced resemble those produced by deoxycortone (D.C.A.). The serum potassium was lowered, blood pressure was raised, and withdrawal of sodium P.A.S. was followed by a diuresis, loss of weight, and lowering of blood pressure. The serum sodium, however, was never found to be abnormal, but plasma chlorides were low on the single occasion when they were measured.

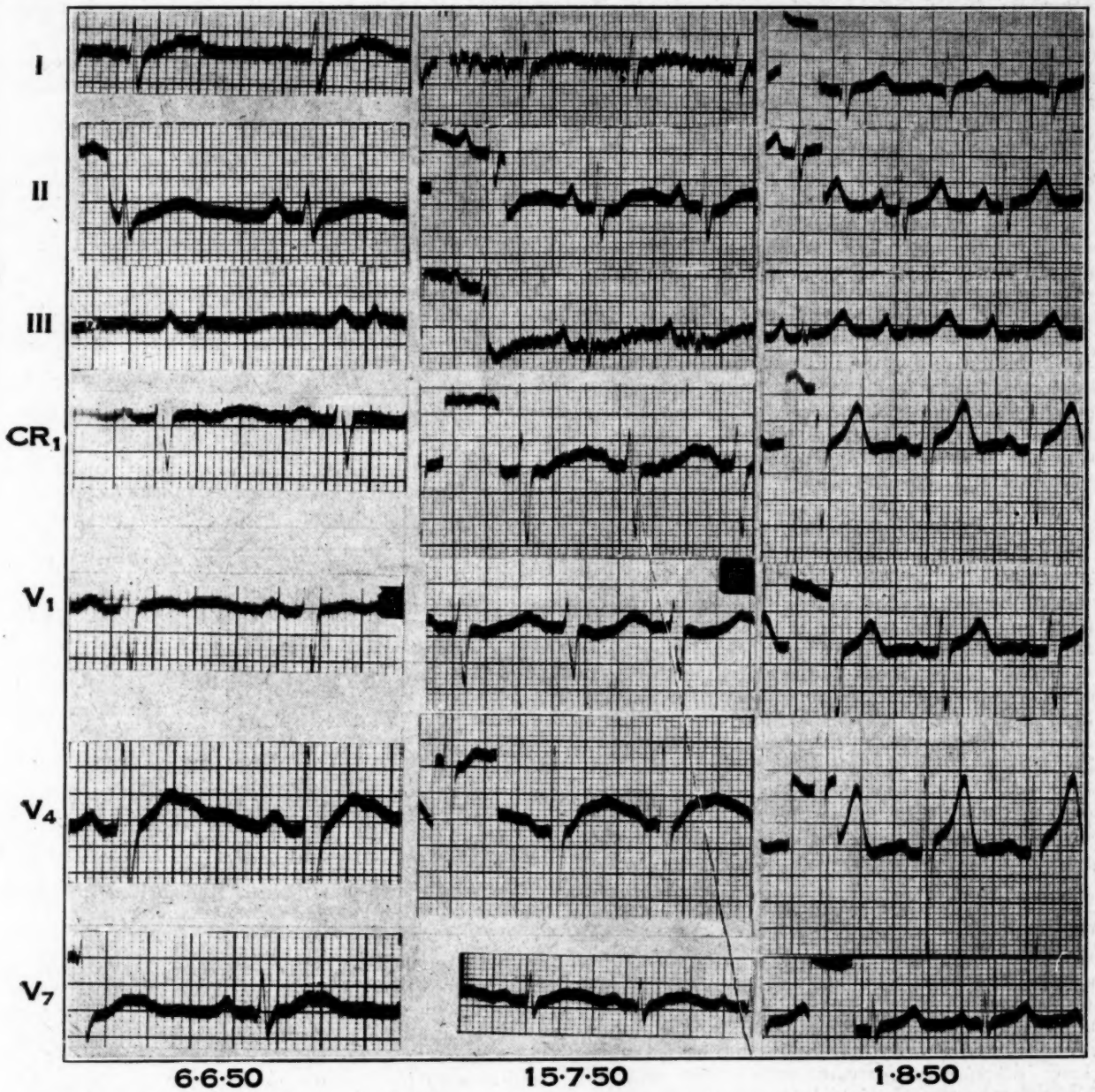
Campbell and Neufeld (1951) attributed the hypokalaemia developing during P.A.S. therapy to an impurity in certain commercial preparations of P.A.S. They found that ext. glycyrrhiz. liq., given in four 1-drachm (3.5-ml.) doses daily with P.A.S., caused a slight lowering of the serum potassium concentration, and that the lowest levels were encountered when impure potassium P.A.S. was administered with liquorice.

If, then, liquorice was responsible for the low serum potassium and the related symptoms, it seems surprising that no other cases than those mentioned have been reported, as liquorice was widely used as a flavouring agent for P.A.S. and other drugs. Individual idiosyncrasy may be an important factor, and, as Borst *et al.* (1950) further point out, not all preparations of liquorice appear to possess this property, which may be related to their origin or to conditions of preparation and storage. P.A.S. is now commonly sold in cachets, so the need for a flavouring agent no longer exists.

It is of particular interest that Groen, Pelser, Willebrands, and Kamminga (1951) have reported satisfactory control of two patients with Addison's disease using liquorice extracts.

Cates (1949) has reported on the occurrence of oedema and potassium loss in combined sodium *p*-aminohippurate and penicillin therapy during the treatment of a case of subacute bacterial endocarditis; he was, however, giving the equivalent of 25.5 g. of sodium by intravenous infusion daily, whereas the two cases here described were having 15 g. of sodium P.A.S. daily, which would contain approximately 2 g. of sodium.

Fluid retention could scarcely be attributed to such a small increment of the sodium intake, nor is it likely to have been responsible for the gross serum potassium deficit.



The most striking changes in the records of June 6 and July 15 are in the prolongation and flattening of the T waves in all leads. The corrected Q–T interval (Ashman and Hull, 1941) was 0.47 sec. on June 6; this had increased to approximately 0.60 sec. on July 15, and had diminished to 0.425 sec. on August 1. Owing to superimposition of P waves on T waves in the record of July 15 it is impossible to measure the Q–T interval precisely, and the figure should therefore perhaps be even higher than that given. The E.C.G. abnormalities found on June 6 evidently occurred before the serum potassium was lowered, as the latter was normal on June 15. Records taken later were identical with those made on August 1 and it is assumed that they represented the normal for the individual. (The normal QTC in the adult male may extend to 0.422 sec.)

Trousseau's Sign

The serum and urinary calcium were normal whenever examined and cannot therefore have accounted for the presence of this sign, unless the plasma protein concentration had been grossly raised.

The relation of Trousseau's sign to hypocalcaemia and hypopotassaemia has been examined in detail in two cases of malabsorption syndrome by Engel, Martin, and Taylor (1949), who found that raising the serum potassium while the calcium content remained low regularly precipitated overt tetany, which could then be abolished by the infusion of calcium. This is in contrast to Case 2, in which Trousseau's sign disappeared when the serum potassium was restored to normal, and it is more likely, therefore, that a change in *p*H was the factor concerned rather than purely a change in the serum calcium:potassium ratio. Lowering of the serum potassium with a normal or raised plasma *p*H would be expected to diminish the tendency for tetany to occur (Lehmann, 1937).

Engel *et al.* (1949) suggest that anoxia, by releasing potassium from cells, may lower the threshold to conduction in the limb below the pressure cuff, and thus convert latent to overt tetany. This would provide an explanation for the absence of Chvostek's sign when Trousseau's phenomenon could be readily elicited. In the presence of a normal serum calcium Trousseau's sign probably occurs only if the plasma *p*H is raised. In the cases described the CO_2 combining power was either raised or in the upper range of normality while this sign

was present. Had the plasma *p*H been determined it is likely that a state of uncompensated metabolic alkalosis would have been revealed. This is known to occur in conditions associated with a low serum potassium—for examp'e, Cushing's syndrome (Kepler, Sprague, Mason, and Power, 1948 ; Teabeaut, Engel, and Taylor, 1950)—and rarely in post-operative patients (Kepler *et al.*, 1948).

Myasthenia

The distribution and nature of the muscular weakness observed with diminished tendon reflexes was similar to that described in familial periodic paralysis in which a low serum potassium content is associated with muscle weakness. Responses to direct muscle electrical stimulation, using a Ritchie-Sneath stimulator, showed a raised threshold during the phase of muscle weakness with all pulse lengths used ; this was lowered appreciably when the serum potassium returned to normal. These findings are of course contrary to those of tetany as exemplified in Erb's sign, and constitute a paradox in the presence of Trousseau's sign.

Electrocardiographic Changes

The records taken on June 6 and July 15 show striking changes compared with that of August 1, when the serum potassium had returned to normal. Subsequent records showed no further change. It is, however, remarkable that the changes seen on June 6 had occurred long before symptoms of hypokalaemia had appeared, or the serum potassium was found to be abnormal. This may be related to changes in intracellular potassium, which at the time were not reflected in the serum. Cates (1949) likewise noted that electrocardiographic changes appeared before the serum potassium fell. At no time were any clinical signs of cardiovascular abnormality found other than the slight rise of blood pressure when the serum potassium was low.

Hypopotassaemia

This has been reviewed by Darrow (1948) and Danowski (1949). Diminished intake of potassium and excessive loss from vomiting, diarrhoea, fistulae, and intestinal aspiration are regarded as prominent causes. Cushing's syndrome, D.C.A. intoxication, and familial periodic paralysis rarely may be responsible. Diabetic acidosis which is being treated with insulin, especially when sodium is also being administered, is likely to show a serum potassium deficit. Occasionally in advanced renal disease potassium depletion may occur. In the two cases described there was no evidence that impairment of renal function could have been responsible for the depletion of their serum potassium.

Summary

Two cases showing marked muscular weakness associated with treatment with sodium P.A.S. and liquorice extract are reported.

In one case the association of such weakness with a low serum potassium was demonstrated.

The occurrence of Trousseau's sign in this condition is noted.

The mechanism involved in the production of such a serum potassium deficit is examined.

I wish to thank Miss E. Gilchrist for the biochemical investigations involved ; Dr. H. Mowat, house-physician, for her careful records ; and Dr. W. I. Card, in whose unit the patient was treated, for his helpful advice and criticism at all times. Miss S. H. Cameron, physiotherapist at the Northern General Hospital, kindly measured the electrical reactions. I also wish to thank Dr. F. E. de W. Cayley for information about his patients and for drawing attention to Cates's (1949) report, and Mr. J. B. Marshall, of the Department of Public Health and Social Medicine, for his advice regarding the statistics summarized in Table II.

References

Ashman, R., and Hull, E. (1941). *Essentials of Electrocardiography*, 2nd ed. Macmillan, New York.
Borst, J. G. G., Gerbrandy, J., Jong, J. C. de, Lenstra, J. B., Molhuysen, J. A., Turner, K. P., and Vries, L. A. de (1950). *Lancet*, **2**, 381.
Campbell, A. H., and Neufeld, O. E. (1951). *Med. J. Aust.*, **1**, 725.
Cates, J. E. (1949). *Clin. Sci.*, **8**, 53.
Cayley, F. E. de W. (1950). *Lancet*, **1**, 447.
Danowski, T. S. (1949). *Amer. J. Med.*, **7**, 525.
Darrow, D. C. (1948). *Bull. N.Y. Acad. Med.*, **24**, 147.
Engel, F. L., Martin, S. P., and Taylor, H. (1949). *Bull Johns Hopk. Hosp.*, **84**, 285.
Groen, J., Pelser, H., Willebrands, A. F., and Kamminga, C. E. (1951). *New Engl. J. Med.*, **244**, 471.
Heard, K. H., Campbell, A. H., Hurley, J. J., and Ferguson, E. (1950). *Med. J. Aust.*, **2**, 606.
Kepler, E. J., Sprague, R. G., Mason, H. L., and Power, M. H. (1948). *Recent Prog. Hormone Res.*, **2**, 345.
Lehmann, J. E. (1937). *Amer. J. Physiol.*, **118**, 613.
Teabeaut, R., Engel, F. L., and Taylor, H. (1950). *J. clin. Endocrinol.*, **10**, 399.

INCIDENCE OF BACT. COLI O GROUP 111 IN SPORADIC INFANTILE GASTRO-ENTERITIS

BY

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AND

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Since the publication of the results of Taylor, Powell, and Wright (1949) into the incidence of *Bact. coli* O group 111 (one hundred and eleven) (*Bact. coli* D433) in gastro-enteritis, some of whose work was carried out at this hospital, we here have continued investigations on similar lines for the past two years. Our results are presented below.

Material and Methods

The period covered was from June 26, 1949, to March 3, 1951. During this time 264 cases of infantile diarrhoea and vomiting were admitted to the gastro-enteritis ward. Rectal swabs were taken from every case on admission and thereafter at intervals of two to four days until their discharge. Thirty individual colonies were picked from the rectal swab plate and tested for slide agglutination with a *Bact. coli* O group 111 K serum prepared in rabbits. If no agglutination was found after 30 colonies had been tested, a mass suspension was made by sweeping a platinum loop across the thickest part of the inoculum and subjected to the agglutinating serum. If any agglutination occurred with such a suspension the remaining discrete colonies were tested until a positive result was obtained. One in ten of the colonies previously identified as *Bact. coli* O group 111 was put up to titre by the standard tube technique.

Results

Cases positive on admission, 89, or 33.4%.

Cases negative on admission, 175, or 66.6%.

Cases positive on discharge, 81, or 30.7%.

Cases negative on discharge, 183, or 69.3%.

Cases positive throughout, 14, or 5.3%.

Cases negative throughout, 106, or 40.2%.

Cases positive on admission, negative on discharge, 42 or 15.9%.

Cases negative on admission, positive on discharge, 33, or 12.5%.

Cases positive on admission, varying throughout, 33, or 12.5%.

Cases negative on admission, varying throughout, 36, or 13.6%.

Cases Positive on Admission.—89 cases, or 33.4% of total, of which 14, or 15.7%, remained positive throughout; 42, or 47.2%, became negative and remained so; 33, or 37.1%, varied throughout.

Cases Negative on Admission.—175 cases, or 66.6% of total, of which 106, or 60.6%, remained negative throughout; 33, or 18.9%, became positive and remained so; 36, or 20.5%, varied throughout.

Cases Positive on Discharge.—81 cases, or 30.7% of total, of which 14, or 17.3%, had been positive throughout; 33, or 40.7%, were originally negative; 34, or 42.0%, varied throughout.

Cases Negative on Discharge.—183 cases, or 69.3% of total, of which 106, or 57.9%, had been negative throughout; 42, or 22.9%, were originally positive; 35, or 19.2%, varied throughout.

The complete variability of these findings appears to us to need no comment.

Control Series

During the period September 16, 1950, to March 3, 1951, each time a new case was admitted to the gastro-enteritis ward a similar case admitted without gastro-intestinal upset to some other ward was swabbed as a control. Each control was swabbed as soon after admission as was practicable, and for the sake of completeness two control series were run—the first under the age of 2, as were all our cases of gastro-enteritis, and the second over the age of 2. The results obtained are shown in Table I, the period having been broken up into four weekly periods. It will be seen that there is notably little difference between the isolations of *Bact. coli* O group 111 from the cases of gastro-enteritis and those from the controls.

TABLE I.—*Cases and Controls from which Bact. coli O Group 111 was Isolated on Admission*

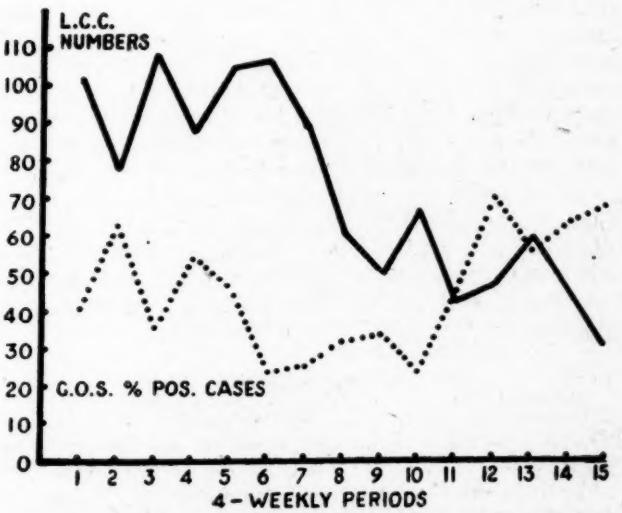
4-weekly Period	Cases of Gastro-enteritis	Under 2 Controls	Over 2 Controls
1	2 of 12 (16·7%)	2 of 12 (16·7%)	4 of 14 (28%)
2	2 ,, 12 (16·7%)	3 ,, 12 (25%)	1 ,, 12 (8·3%)
3	1 ,, 15 (6·7%)	2 ,, 15 (13·4%)	0 ,, 15
4	2 ,, 15 (13·4%)	3 ,, 15 (20%)	3 ,, 15 (20%)
5	3 ,, 16 (18·8%)	3 ,, 16 (18·8%)	0 ,, 16
6	2 ,, 15 (13·4%)	4 ,, 15 (26·8%)	3 ,, 15 (20%)
Totals	12 ,, 85 (14%)	17 ,, 85 (20%)	11 ,, 87 (12·6%)

L.C.C. Notifications of Gastro-enteritis

During the period from June 26, 1949, to August 19, 1950, we were able to obtain from the L.C.C. Health Department the number of cases of gastro-enteritis notified to them. The cases admitted to the Hospital for Sick Children were essentially comparable in that they were drawn from the same area, but possibly not so comparable in that naturally the more severe cases were likely to have been sent to hospital, and therefore our cases would be more severe than the average notified. It seemed worth while, however, to correlate the numbers of notifications with the number of hospital cases showing *Bact. coli* O group 111 on admission. Since the number of beds available for cases of gastro-enteritis was limited we have expressed the positive Great Ormond Street cases as a percentage of the total admitted. The L.C.C. cases were included in the four-week period in which the actual illness arose, and not according to the date of each notification. The total L.C.C. cases and Great Ormond Street percentages are shown in Table II. The Chart shows a completely inverse relationship between the total number of cases of gastro-enteritis in the L.C.C. area and the percentage of our sample of this total from whom *Bact. coli* O group 111 was recovered on admission.

TABLE II.—*Total Cases Notified to the London County Council, and Those Admitted to Great Ormond Street, for Each Four-week period from June 26, 1949, to August 19, 1950*

Period	Total L.C.C. Notifications	Total G.O.S. Cases	G.O.S. Cases with *Bact. coli* O Group 111 on Admission	
			No.	Percentage of Total
1	102	15	6	40·0
2	77	8	5	62·5
3	108	14	5	35·7
4	87	13	7	53·8
5	104	9	4	44·4
6	106	13	3	23·1
7	88	12	3	25·0
8	60	16	5	31·3
9	49	6	2	33·3
10	66	13	3	23·1
11	41	9	4	44·4
12	46	10	7	70·0
13	59	9	5	55·5
14	44	8	5	62·5
15	30	9	6	66·7



Graph showing reverse relationship between cases of gastro-enteritis in the L.C.C. area and the percentage of cases at Great Ormond Street Hospital from which *Bact. coli* O group 111 was recovered on admission.

Discussion

We are well aware of the findings of specific agglutinable types of *Bact. coli* in association with infantile diarrhoea and vomiting, recently epitomized by Taylor (1951) and Rogers (1951), and the support which has been forthcoming for their work from almost every other country in the world. It is true that we have investigated only the incidence of *Bact. coli* O group 111, and

have not taken into account the beta and other agglutinable types of *Bact. coli*. Even so, we are perplexed by the discrepancy between our findings and those of others, and record the figures for what they are worth.

The incidence of this particular strain of *Bact. coli* in our cases is much lower than we had expected, and we thought that our 30 individual colonies slide-agglutinated would have given us a higher percentage of positive results than the three or four colonies reported as having been examined by some other workers. A false positive slide agglutination is more likely than a false negative, and were our findings to be explained on technical grounds we would have expected an even higher incidence than was obtained. Similarly, from a study of the published work we expected our control series of cases—as comparable as we could get them, except that there was no gastro-intestinal disorder—to have a much lower incidence than was found.

Taylor (1951) and others have emphasized that their greatest isolation of *Bact. coli* O group 111 was obtained in epidemics, whereas our cases, with the exception of the few arising *de novo* in another ward of the hospital and subsequently transferred to the gastro-enteritis unit, cannot be regarded as epidemic cases. The L.C.C. cases are probably mostly sporadic; and here again, to put it no stronger, our figures show that there is no correlation between the total number of cases notified and the percentage incidence of *Bact. coli* O group 111 in our hospital cases.

We are unable to offer any explanation why our findings are so different from those of others, unless such is to be found in some difference between the epidemic and sporadic disease, or an enhancement of virulence of a causal organism leading to an epidemic Even so, we are disappointed that an organism impliedly associated with the pathogenesis of epidemic gastro-enteritis has in our experience been so infrequently found in sporadic cases of what appears to be the same disease. We are perturbed, also, by the incidence of the same potential pathogen in the rectal swabs of healthy babies of the same age group, an incidence for all practical purposes identical over a period of six months with that found in our cases of sporadic infantile gastro-enteritis.

There has been a tendency recently to regard these agglutinable strains of *Bact. coli* as the *cause* of gastro-enteritis, and, while we do not suggest that there is no relationship between the organism and the disease, our results do not support the idea that the particular organism we have investigated is causal.

Summary

Figures are presented of the isolation of *Bact. coli* O group 111 (D433) from 264 cases of sporadic infantile gastro-enteritis observed over a period of two years.

In a shorter control series this organism was isolated as often as in the cases of the disease.

No correlation was found between the total number of cases notified to the L.C.C. and the percentage of cases in which the organism was found on admission to the Hospital for Sick Children.

We are grateful to Dr. Joan Taylor for advice, to Sir Allen Daley for the L.C.C. notifications, and to the physicians of the Hospital for Sick Children for access to their cases.

References

Rogers, K. B. (1951). *Proc. roy. Soc. Med.*, **44**, 519.
Taylor, J. (1951). Ibid., **44**, 516.
—— Powell, B. W., and Wright, J. (1949). *British Medical Journal*, **2**, 117.

SO-CALLED ACCIDENTAL MECHANICAL SUFFOCATION OF INFANTS

BY

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During 1940–9 in England and Wales the average annual number of deaths ascribed to the accidental mechanical suffocation of infants aged under 1 year was 620. There has for some time been considerable doubt whether the deaths so registered are in fact due to the cause alleged. Brend (1915) believed that many supposedly suffocated infants died from natural causes, and gave some statistics that lent support to his suggestion. Davison (1945), coroner for the City of Birmingham, ordered post-mortem examinations to be carried out by skilled pathologists on every case in which asphyxia was considered to be a possible cause of death in an infant; he found that out of 318 cases only 24 died from asphyxia caused mechanically. In the U.S.A., Werne and Garrow (1947) investigated the deaths of 167 infants where accidental mechanical suffocation was alleged to be the cause. In 43 the gross findings were adequate to establish a natural cause of death; of the remaining 124 cases, microscopical studies showed natural causes of death in many. In Australia, Bowden (1950) recorded the post-mortem findings in 40 cases of sudden death in infants, nearly all in bed. Morbid changes were found in all of them.

Though the pathological evidence indicates that some infant deaths ascribed to accidental mechanical suffocation are much more probably due to disease, it does not enable us to estimate what proportion. Suffocation may leave no signs discernible in an infant after death, and it is possible that an infant suddenly smitten with pneumonia, for example, might succumb to asphyxia from pressure of its sleeping mother's breast or from a pillow in its cot, while a healthy infant would have no difficulty in surviving either hazard. But certainly a considerable proportion of the cases described showed lesions sufficient to account for death without any need to invoke mechanical suffocation as a cause when there was no firm evidence of it.

The numbers of deaths in England and Wales recorded by the Registrar-General in the periods 1921–30, 1931–9, and 1940–9, distinguished by sex of infants and circumstances of death, are shown in Table I. Because of changes in the method of classification, the actual numbers of deaths in the first two periods are not strictly comparable with those in the third.

Table I.—*Deaths from Accidental Mechanical Suffocation in Infants in Three Periods, 1921–49, England and Wales*

Years	In Bed		In Cot, Cradle, etc.		By Food		Other		Total	
	M	F	M	F	M	F	M	F	M	F
1921–30	1,810	1,622	171	112	214	146	203	185	2,398	2,065
1931–9	1,031	791	311	192	313	248	45	32	1,700	1,263
1940–9	1,165	892	1,014	638	1,258	907	185	144	3,622	2,581

Sex Ratios

A feature of any cause of death is the distribution of the deaths between males and females—that is, the sex ratio of the deaths. This distribution is as characteristic of a particular cause of death as, for example, the age

distribution of the people who die from that cause. Like the age distribution it varies from year to year or decade to decade in accordance with certain definable attributes of the population exposed to the risk of death from that cause, and it is also subject to chance variation because of the influence of many small and incalculable factors acting in a random manner. If the number of deaths from which the sex ratio is calculated is small, chance variation tends to obscure the operation of the main factors that determine the size of the sex ratio. As the sample becomes larger the effect of certain important factors becomes apparent. The two main factors concerned here are the sex distribution of the population exposed to risk and the differing susceptibility, characteristic of each sex, to death from a particular cause. When comparing the sex ratios of deaths from two or more causes in the same population, we find that the main effective reason for the difference between them is the fact that the deaths are caused by different agents.

Sex ratios are expressed here in the form of male deaths per 100 total deaths. In Table II these ratios are given for deaths in three defined categories of deaths from accidental mechanical suffocation recorded by the Registrar-General.

TABLE II.—*Percentage Male Deaths from Accidental Mechanical Suffocation in Infants in Three Periods, 1921–49, England and Wales*

Years	In Bed	In Cot, Cradle, etc.	By Food	Other	Total
1921–30 ..	52·74	60·42	59·44	52·32	53·73
1931–9 ..	56·59	61·83	55·79	58·44	57·37
1940–9 ..	56·64	61·38	58·11	56·23	58·39

It will be seen that, in the three periods considered, deaths "in cot, cradle, etc." showed a higher percentage of males than did deaths "in bed" or "by food." In the period 1921–30 the difference between the sex ratio of cot deaths and that of bed deaths is 7.68 and is statistically significant (S.E. = 3.09; difference/S.E. = 2.5). In 1931–9 the comparable difference is 5.24 (S.E. = 2.49; difference/S.E. = 2.1), which is statistically significant, and in 1940–9 it is 4.74 (S.E. = 1.63; difference/S.E. = 2.9), also statistically significant. As to the difference between cot and food deaths, in 1921–30 it is 0.98 (S.E. = 3.89; difference/S.E. = 0.3); in 1931–9 it is 6.04 (S.E. = 3.02; difference/S.E. = 2.0); and in 1940–9 it is 3.27 (S.E. = 1.60; difference/S.E. = 2.0). Thus in two of the periods the differences between cot and food deaths are significant at the 5% level, while in 1921–30 the difference does not attain significance. The probable reason for its not doing so is that comparatively few deaths in cot and by food were recorded in that period. The standard error of the sex ratios is therefore rather high; for the sex ratio of the food deaths it is 2.59.

The conclusion suggested by these differences is that many of the cot deaths are caused differently from deaths in bed or by food. Yet all are alleged to be due to the same cause—accidental mechanical suffocation.

The Cot Deaths

Since pathological investigations have indicated that many babies supposedly suffocated probably died from natural causes, we should expect to find that the sex ratio of total deaths from accidental mechanical suffocation is considerably higher than that of live births and approaches rather the sex ratio of total infant deaths. The relevant figures are set out in Table III.

TABLE III.—*Sex Ratios (Percentage Males) of Live Births, Total Infant Deaths, and Deaths from Accidental Mechanical Suffocation in Three Periods, 1921–49, England and Wales*

Years	Live Births		Infant Deaths		Deaths from Accidental Mechanical Suffocation	
	Sex Ratio	S.E.	Sex Ratio	S.E.	Sex Ratio	S.E.
1921–30	51·10	0·019	57·61	0·069	53·73	0·75
1931–9	51·27	0·021	57·71	0·087	57·37	0·91
1940–9	51·48	0·019	57·68	0·087	58·39	0·63

In the two later periods our expectations are fulfilled. But for 1921–30 the sex ratio of deaths from suffocation is surprisingly low. In this decade there were proportionately more deaths "in bed" than in the other two periods, and it is the sex ratio of these deaths that chiefly determines the size of the sex ratio for all deaths from accidental mechanical suffocation. Deaths in bed then comprised 76.9% of all deaths from suffocation, while in 1931–9 they comprised 61.5%, and, in 1940–9, 33.2%. Probably many of the deaths genuinely due to mechanical suffocation are to be found among those classified as having occurred in bed, the suffocation being caused by another occupant of the bed. Since the sex ratio of such deaths is likely to be considerably lower than the sex ratio of deaths from infectious diseases, the inclusion of a substantial number of them in the category of death from accidental mechanical suffocation, together with the deaths from infectious diseases that are also undoubtedly included there, will lower the sex ratio of the composite group. It is impossible to say how many of the deaths were in fact due to suffocation, but there may well have been more then than later, for antenatal clinics and other sources of education were then sparser.

But the main problem is why deaths from suffocation in cots should have a higher sex ratio than those in beds or by food. It seemed worth while considering whether the sex ratio of cot deaths was higher than the sex ratios of the others because the population at risk had a different sex ratio. This could happen if the cot deaths were of infants who died soon after birth and the other deaths were of infants later in the first year of life, when deaths from other causes would have reduced the excess of males over females under 1 year of age in the population. To test the extreme case, adjusted figures were obtained in the following way: Cot deaths were first assumed to have occurred in a population whose sex composition was that of the live births in each period: the numbers of them were then reduced to the numbers there would have been if they had occurred at the same rate in a population whose sex composition was that of infants at the end of one year's losses from infant deaths. A new sex ratio was computed from the adjusted figures. The calculations carried out are expressed symbolically as follows:

S = Number of suffocation deaths in cot
B = Number of live births
D = Number of all infant deaths
Subscripts M and F = male and female

$$S'_M = S_M \times \frac{B_M - D_M}{B_M}$$

$$S'_F = S_F \times \frac{B_F - D_F}{B_F}$$

$$\text{Adjusted sex ratio} = \frac{S'_M}{S'_M + S'_F} \times 100$$

By this means the adjusted sex ratios were found to be 59.94 in 1921–30, 61.45 in 1931–9, and 61.10 in 1940–9.

Clearly the reduction effected on this assumption is negligible.

The disparity between cot deaths and the others is probably a true one. A likely explanation of it is that the cot deaths are nearly all due to natural causes—and causes that show a high sex ratio—while the bed and food deaths include relatively many more that are genuinely caused by suffocation. Accidents are as likely to befall male as female infants in the circumstances considered here, though it is quite possible that there is some sex distinction in the ability to survive them. But this distinction would not be notably higher in the cot than in the bed.

Diseases Causing Sudden Death

The sex ratios of deaths from certain conditions apt to attack infants with great rapidity, and mentioned as having been found at necropsy in the pathological investigations, were calculated for the periods in question here, and are listed in Table IV.

TABLE IV.—*Sex Ratios of Infant Deaths from Certain Causes in Three Periods, 1921–49, England and Wales*

Cause of Death	Sex Ratio		
	1921–30	1931–9	1940–9
Acute nephritis	59·85	61·09	64·33
Diseases of ear and mastoid antrum	58·86	60·18	60·29
Enteritis and diarrhoea	59·33	59·70	59·47
Congenital malformation of heart	57·89	60·18	58·27
Influenza	59·10	58·72	58·29
Bronchopneumonia	58·03	58·14	57·28
Lobar pneumonia	58·92	58·49	56·37
Bronchitis	57·65	57·29	58·42
Meningitis (non-meningococcal)	58·11	58·19	57·45

As can be seen by comparison with Table III, nearly all these sex ratios are above the sex ratios of total infant deaths in the three periods. The sex ratios of deaths from the first three causes listed approximate closely to the sex ratios of cot deaths from accidental mechanical suffocation. To conclude that acute nephritis, diseases of the ear and mastoid, and diarrhoea and enteritis are the chief causes of death in cases of so-called suffocation in cots would be rash, but certainly diseases of the ear and mastoid are often found in cases of suspected or supposed suffocation. Werne and Garrow (1947), in their 167 cases already referred to, considered that the gross findings at necropsy were adequate to establish a natural cause of death in 43; of these, 20 had mastoiditis and otitis media, and another had bronchopneumonia and otitis media. It is not clear how many of the other cases showed microscopical evidence of natural causes of death, but "complete microscopical studies as a rule showed acute inflammation of the respiratory tracts" in association with other lesions. In view of the fact that deaths from acute nephritis show a notably high sex ratio it is of interest to note that Werne (1942), discussing the pathology of 50 infants who died unexpectedly, stated that many of them showed glomerular lesions.

Bowden (1950) found in his 40 cases 7 cases of otitis media, all associated with pneumonia or bronchitis, 2 cases of enteritis, and 2 cases of subacute nephritis. Some kind of respiratory infection was commonly found.

Out of the 318 cases discussed by Davison (1945), 77 had otitis media with bronchopneumonia or respiratory disease and 8 otitis media with mastoiditis. There were also 2 cases of enteritis, 1 of congenital heart disease, and 1 of meningitis. The largest group of his cases was 152 with bronchopneumonia, capillary bronchitis, and bronchiolitis, without complications. In 24 cases death was attributed to asphyxia by mechanical means, and in 11 to asphyxia by inspiration of vomit.

It yet remains rather surprising that the sex ratio of the cot deaths from suffocation should lie consistently between 60 and 62. It would hardly be likely to do so if the great majority of these deaths were due to uncomplicated respiratory infections, though still less likely is it that many of them were due to mechanical suffocation. Probably otitis media and mastoiditis comprise the commonest causes of death here, and Werne's findings suggest that acute nephritis is present more often than it is diagnosed.

Changes in Death Rates

The Registrar-General (1951) has pointed out that the annual death rates from accidental mechanical suffocation in infants tended to increase from 1931 to 1947 (the last year that he was reviewing). This increase, in so far as it includes rates for the years 1931–9, must be accepted with caution, for from 1940 onwards the method of classification has changed, deaths from suffocation on which coroners' "open verdicts" were given being assigned to this category instead of to a separate one. Whether there was a real increase in the death rates during the decade 1940–9 as compared with the period 1931–9 is therefore open to slight doubt, but the last column of Table V shows that the death rate for 1940–9 (0.87 per thousand live births) was apparently much higher than that for the previous nine years (0.54).

TABLE V.—*Deaths and Death Rates from Accidental Mechanical Suffocation in Infants in Certain Periods, 1921–49, England and Wales*

	No. of Deaths					Rate per Thousand Live Births				
	Bed	Cot	Food	Other	Total	Bed	Cot	Food	Other	Total
1921–30	3,432	283	360	388	4,463	0·48	0·04	0·05	0·05	0·63
1931–9	1,822	503	561	77	2,963	0·33	0·09	0·10	0·01	0·54
1940..	192	99	137	18	446	0·32	0·16	0·23	0·03	0·73
1941..	273	100	131	32	536	0·47	0·17	0·23	0·06	0·93
1942..	218	136	141	10	505	0·33	0·21	0·22	0·02	0·78
1943..	166	168	120	33	487	0·24	0·25	0·18	0·05	0·71
1944..	240	170	180	51	641	0·32	0·23	0·24	0·07	0·85
1945..	219	155	183	43	600	0·32	0·23	0·27	0·06	0·88
1946..	212	198	270	45	725	0·26	0·24	0·33	0·05	0·88
1947..	242	231	385	53	911	0·27	0·26	0·44	0·06	1·03
1948..	170	189	312	25	696	0·22	0·24	0·40	0·03	0·90
1949..	125	206	306	19	656	0·17	0·28	0·42	0·03	0·90
1940–9	2,057	1,652	2,165	329	6,203	0·29	0·23	0·30	0·05	0·87

During 1940–9 the rates for the years individually rise very slightly, though irregularly, and it is too soon to attach much importance to such trend as is seen. But there does seem to be a distinct post-war rise in the death rate from suffocation "by food" after a small decline during the war. Whether there has been a post-war decrease in breast-feeding is problematical, but Moncrieff (1950) has drawn attention to a decline in the practice in recent years. If breast-feeding has declined in the last few years—and it is a matter only for speculation—the cause of the rising death rates might be sought there, for babies have been suffocated by being left on their own to suck from a bottle; they rapidly ingest the milk, regurgitate some of it, and inhale the vomit. It is a dangerous practice—possibly common—and worth while preventing so far as is possible by instruction to mothers. Coroners may be able to elucidate the true cause of these deaths and by publicity help to prevent them.

The death rates from suffocation "in bed" show a tendency to decline recently. Again this might be due to more bottle-feeding, with the result that fewer mothers go to sleep and thereby suffocate their babies while breast-feeding them in bed. But there seems to have been during the decade a slight rise in the death rates from suffocation "in cot, cradle, etc.," and the two may be related. Higher wages have enabled more parents than formerly to buy cots if they wish to do so, and the babies may be placed in them in preference to beds containing other occupants.

Conclusion

The importance of precisely ascertaining the cause before attributing the death of a baby to accidental mechanical suffocation lies in the effect that such a diagnosis may have on the parents. Few would not bitterly reproach themselves for having contributed, however unwittingly, to the death of their baby. Yet many whose baby's death is so recorded, even though ignorant of the dangers of taking a baby into their bed, or laying it face down on a soft pillow, are in fact innocent of allowing their baby to die of suffocation. Especially is this true when babies are found dead in cots and cradles, as the sex ratios show.

Summary

The sex ratios of infant deaths from accidental mechanical suffocation in various circumstances suggest that the causes of death in cots and cradles differ considerably from the causes of death in bed and by food. Published evidence is cited indicating that in any case only a minority of these deaths are due to suffocation.

Recently, death rates for suffocation "in bed" have declined, while those for suffocation "in cot, cradle, etc.," and "by food" have risen.

No infant's death should be attributed to accidental mechanical suffocation unless there is clear positive evidence of it.

REFERENCES

Bowden, K. (1950). *Med. J. Aust.*, **1**, 65.
Brend, W. A. (1915). *An Inquiry into the Statistics of Deaths from Violence and Unnatural Causes in the United Kingdom*. Griffin, London.
Davison, W. H. (1945). *British Medical Journal*, **2**, 251.
Moncrieff, A. (1950). Ibid., **2**, 795.
Registrar-General (1951). *Statistical Review of England and Wales for the Two Years 1946-7*, Text, Vol. 1, Medical. London.
Werne, J. (1942). *Amer. J. Path.*, **18**, 759.
—— and Garrow, I. (1947). *Amer. J. publ. Hlth*, **37**, 675.

The October issue of *Industrial Health Monthly*, a publication of the Federal Security Agency (Public Health Service) from Washington, D.C., contains an article "Who's an Amputee?" which discusses the practical problems of artificial-limb fitting as seen in the U.S.A. Although there are about 900,000 civilians who have had an amputation, and about 40,000 new amputations are performed every year, only half of them are able to use artificial limbs. After the second world war the Veterans' Administration investigated the reasons for failure to use artificial limbs, and found two chief reasons. One was educational: the patient was not taught how to use his limb in the most comfortable and efficient way. The other was that after operation the stump became fixed. After amputation the patient was returned to bed and a soft pillow placed under the thigh stump so that it stuck up in the air, and in 10 days it was already stiff in this position. Then the patient went home to wait in a wheel-chair till his new leg was ready. When it arrived, with one hip fixed he had to tilt his spine and pelvis if he was to walk with it, and this quickly produced pains and complaints about the artificial leg.

EFFECT OF CIGARETTE-SMOKING ON BLOOD FLOW THROUGH THE HAND

BY

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It is generally held that tobacco-smoking causes a decrease in the skin blood flow. Lampson stated in 1935, for example, that following the inhalation of the smoke from one cigarette the rate of peripheral blood flow was at least halved and remained depressed for about 60 minutes. If the smoke was not inhaled the vasoconstrictor response was almost as great but the decrease lasted only 15 minutes. He attributed these results to the pharmacological action of the tobacco. Roth, McDonald, and Sheard (1944) reviewed previous work, and in a further investigation on six normal subjects showed that after smoking two "standard" cigarettes the cutaneous temperature of the extremities of all the subjects decreased. They concluded that "the smoking of standard cigarets should be avoided in the presence of peripheral vascular disease."

A reflex vasoconstriction in the digits, however, follows deep inspiration (Bolton, Carmichael, and Stürup, 1936; Gilliatt, 1948), and Mulinos and Shulman (1940) were the first to point out that the primary factor in the causation of the decreased blood flow might be the deep breathing associated with the inhalation of the tobacco smoke, rather than the action of any substance contained in the tobacco.

It seemed to be worth while investigating whether the rate of smoking had any effect on the blood flow through the hand, and, if so, whether the flow was affected by what might be regarded as a normal rate of smoking. Evidence will be presented which suggests that when cigarette smoke is inhaled at a rapid rate there is a marked and continuous decrease in the blood flow. However, when smoking is carried out at approximately the normal rate there is only a transient decrease in hand blood flow at the moment of inhalation. In the former instance the decrease is mainly pharmacological, due to the action of the tobacco, but in the latter it is mainly physiological, due to the associated deep breath on inhaling.

Methods

The depth of respiration was recorded by means of two stethographs, one at the level of the fourth intercostal space and one at the level of the umbilicus, connected to a common volume recorder. Preliminary calibration of the system against collection and measurement of expired air showed a nearly linear relationship between the amplitude of the excursions and the tidal air.

Hand blood flows were recorded by means of a venous occlusion plethysmograph (Barcroft and Edholm, 1945) filled with water at 32° C., the principle being that described by Brodie and Russell (1905) and Hewlett and Van Zwaluwenburg (1909).

The subjects were young healthy males with normal cardiovascular systems. They smoked on the average 10–20 cigarettes a day. All were accustomed to hand plethysmography, and were told the details of the

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experimental procedure some time before observations were begun. This was to reduce to a minimum any psychological stimuli which can lead to marked variations in hand blood flow. They rested in the laboratory, the temperature of which was maintained at about 24–25° C., for half to one hour before the experiments began. During experiments the subject sat in a chair with the right hand in a plethysmograph. The observations were made in the afternoon or evening, and in all cases the subjects had smoked cigarettes at their accustomed intervals throughout the day.

A standard brand of British cigarette containing a mixture of Virginian and Empire tobacco was used throughout. In some of the experiments the subject inhaled at intervals of a minute. In other experiments the interval between inhalations was 20 seconds. In each experiment the actual smoking was preceded by a period of imitation smoking, in which the same technique was adopted except that the cigarette was unlit. The hand blood flow was recorded every 15 seconds.

The routine procedure was: 10 minutes control period, 10 minutes imitation smoking, 10 minutes control, 10 minutes smoking, 10 minutes control.

Results

When each subject was asked how often he normally inhaled during smoking the usual reply was, "Every 15 seconds," and this rate was therefore adopted in the preliminary series of experiments. However, generalized reactions, notably dizziness, nausea, and a feeling of faintness, commonly followed inhalation at this rate. Two subjects would probably have lost consciousness if the experiment had not been terminated. A series of observations was therefore made to determine the normal rate of inhalation. Fifty males were surreptitiously observed inhaling tobacco smoke in buses, restaurants, and public and private houses. The average rate of inhalation was determined for each subject, and the results are shown in Fig. 1. Sixteen of these were observed from start to finish of the cigarette, 24 for at least seven consecutive inhalations, and 10 for six consecutive inhalations. The average intervals between inhalations in the three groups were 67, 66, and 68 seconds respectively. The average of all observations was 66 seconds. The shortest individual average interval was 43 seconds, and yet when some of these people were asked what they thought was their normal rate of inhalation the usual reply was, "About once every 15 seconds." On the basis of these findings the inhalation rate adopted in the present experiments was once every minute, which was a convenient approximation to the mean of 66 seconds for the 50 subjects.

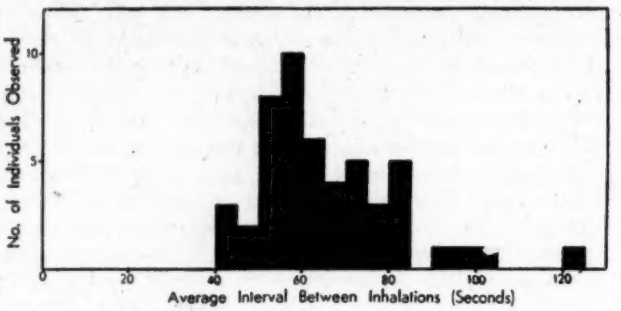

Fig. 1.—The average rate of inhalation of cigarette smoke in 50 male subjects (for details see text).

The average of the hand blood flows obtained in 12 subjects who inhaled at this rate is shown in the top half of Fig. 2. It will be seen that during the period of imitation smoking a sharp drop in hand blood flow occurred at intervals of a minute—that is, during the imitation inhalation—and that the flow 15 seconds later

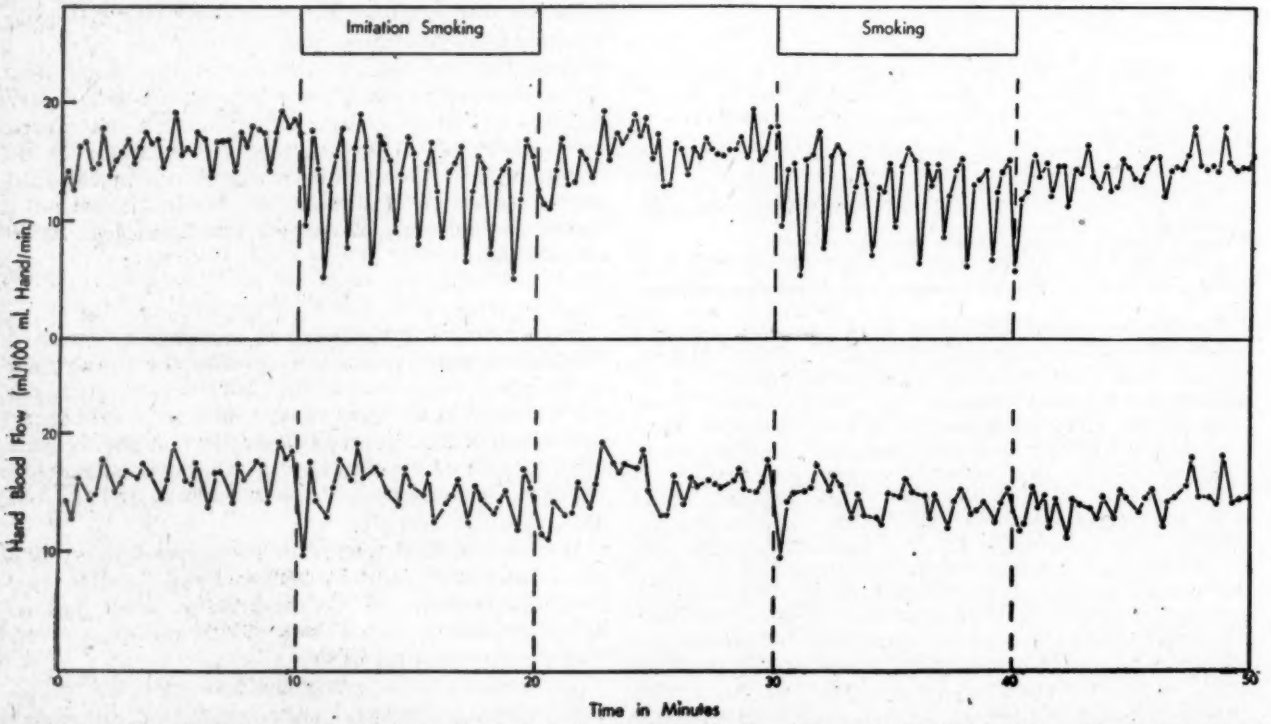

Fig. 2.—Upper half: A comparison of the effects of smoking and imitation smoking on the hand blood flow. Composite graph of the results obtained on 12 subjects. Inhalations every minute. At the time of inhalation there is a transient decrease in flow, both during smoking and imitation smoking. Lower half: The flows recorded at the moment of inhalation of the tobacco smoke and the corresponding flows during the imitation period have been removed to illustrate that the general level of hand blood flow remains substantially unchanged with either smoking or imitation smoking at this rate.

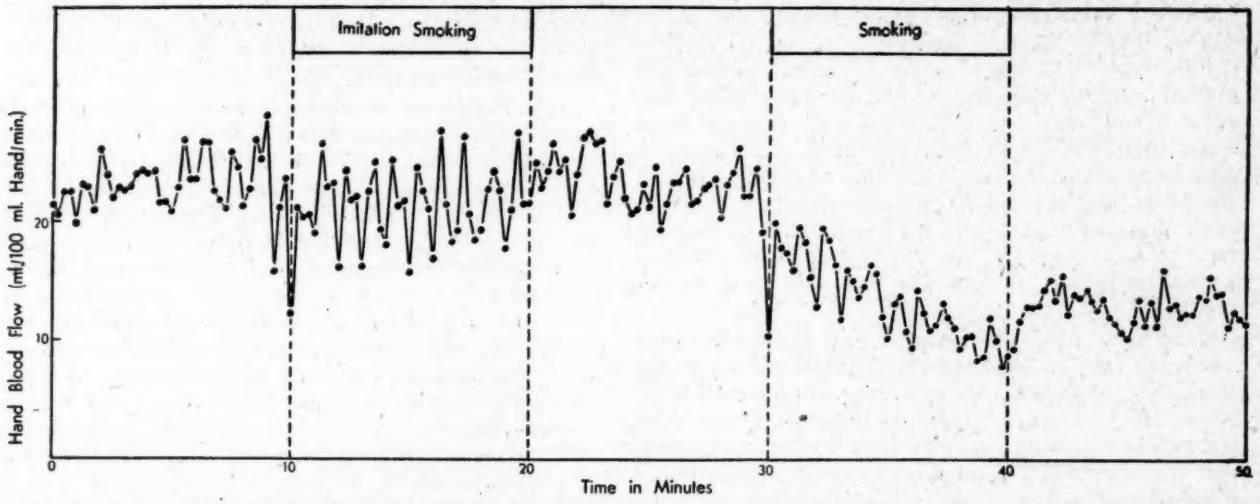

FIG. 3.—A comparison of the effects of smoking and imitation smoking on the hand blood flow. Composite graph of the results obtained on six subjects. Inhalations every 20 seconds. Note the gradual well-marked decrease in flow during the smoking period as compared with the imitation smoking period.

had returned to about the previous level. Very similar changes occurred during the smoking period, the blood flows decreasing to the same extent during inhalation, with an equally rapid recovery.

The stethographic records showed no significant difference between the depths of inhalation during these two periods. A comparison of the individual blood-flow records showed similar results, but the random fluctuations in hand blood flow were greater at all times.

In the bottom half of Fig. 2 the same results are shown, with the exception that the reading showing the sharp drop in flow during each real or imitation inhalation has been omitted. It can be seen that the general blood-flow level has not substantially altered throughout the whole 50-minute period of observation. The sharp drop in flow at the beginning of the smoking and imitation smoking period was due to placing a cigarette between the subjects' fingers, and is a good example of how transient vasoconstriction of the hand blood vessels may result from very minor stimuli.

The general hand blood-flow level varied from subject to subject, so that all degrees of vasodilatation are represented in the composite results.

Blood-pressure recordings were not made during these experiments, as it has been shown by Roddie (1951) that the rapid inflation of a blood-pressure cuff on one arm causes a transient decrease in hand blood flow on the opposite side. Further, there is no adaptation to this stimulus even with repeated application in trained subjects. It was felt that the additional vasoconstriction resulting from this stimulus would make the interpretation of the records difficult. A separate series of blood-pressure and pulse-rate recordings was made on six subjects before, during, and after inhaling cigarette smoke once a minute. The blood pressure was recorded by the auscultatory method. In no case was there a significant change in the blood pressure or pulse rate.

In order to determine the effects of smoking in excess of the normal rate the experiments were repeated on 6 of the 12 subjects, the routine being the same except that the imitation inhalations and the inhalations of the tobacco smoke were carried out at 20-second instead of at one-minute intervals. At this rate the subjects smoked about 1¼–1½ cigarettes in the 10 minutes. The composite results are shown in Fig. 3. There was in all cases a marked gradual decrease in hand blood flow during the period of smoking as compared with the period of imitation smoking, in spite of the fact that in this series the average depth of inhalation during the imitation was somewhat greater than during the smoking. Two of the subjects felt faint towards the

Table Showing the Effect of Inhaling Cigarette Smoke at 20-second Intervals on Hand Blood Flow, Blood Pressure, and Pulse Rate

Subject	Decrease in Hand Blood Flow	Average Blood Pressure (mm. Hg)						Average Pulse Rate (Beats per min.)		
		Basal		During Smoking		Increase				
		Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	Before Smoking	During Smoking	Inc.
1	66%	126	78	128	81	2	3	65	76	11
2	60%	116	71	116	76	0	5	70	76	6
3	56%	133	80	147	100	14	20	64	64	0
4	29%	114	69	117	74	3	5	83	96	13
5	51%	120	78	122	80	2	2	76	86	10
6	62%	115	75	118	75	3	0	78	88	10
Average	54%	121	75	125	81	4	6	73	81	8

The percentage decrease in hand blood flow has been calculated from the average flow in the five-minute period preceding smoking and the average flow during the last five minutes of smoking.

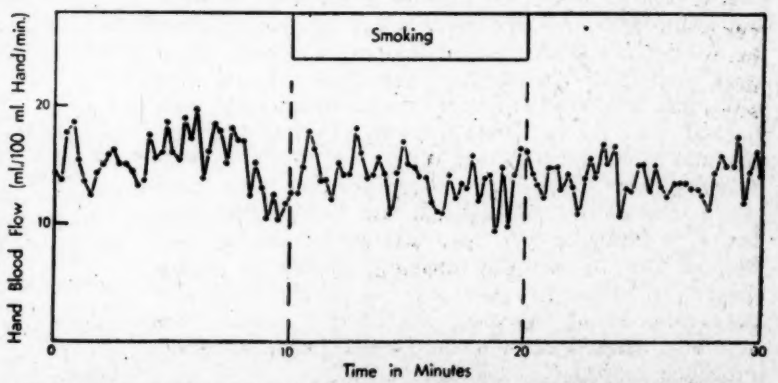

FIG. 4.—Composite result of six experiments which illustrate that the general level of hand blood flow remains unaltered as a result of cigarette-smoking without inhalation of the tobacco smoke.

end of the smoking period. Blood-pressure and pulse-rate recordings made on separate occasions on each of the six subjects during smoking at 20-second intervals showed variable results (see Table). The pulse rate generally increased by 10–12 beats a minute and there was a slight increase in blood pressure. The same two subjects as before felt faint and one of them showed a rise of 14 mm. Hg and 20 mm. Hg in systolic and diastolic pressure respectively, with no alteration in pulse rate. Repeat tests on five of these subjects smoking a common brand of American cigarette gave similar results.

Hand blood-flow measurements were also made during which the subjects kept the cigarette continually in the mouth for 10 minutes, puffing at frequent intervals without inhaling. Six of the original 12 subjects were used, and composite results are shown in Fig. 4. It is clear that no decrease in blood flow occurred with this type of smoking.

Discussion

The present results at first might appear to be at variance with many of those already reported, but the reason for the discrepancy seems to be the difference in the frequency of inhalation. In order to determine the effect of normal cigarette-smoking on the circulation, it is essential that the subject should inhale at his normal rate, and it appears from the literature that in the past insufficient attention has been given to this point. As the average person is incapable of estimating his normal rate, this must be decided by surreptitious observation. As a result of such observations an inhalation rate of once a minute was chosen for the present experiments. The inhalation of tobacco smoke at this rate leads to a sudden transient diminution in hand blood flow at the moment of inhalation, the flow returning to the previous level when the normal depth of breathing is resumed. Similar changes occur when inhalations of the same extent are carried out with an unlit cigarette, and thus the transient diminution appears to be due to the physiological effects of the deep breath rather than to the pharmacological action of the substances in the tobacco smoke. In addition, smoking at this rate causes little or no alteration in blood pressure or heart rate.

Inhalations every 20 seconds, however, lead to a well-marked decrease in flow during smoking. This cannot be explained by the greater number of deep inhalations, as there was no such decrease during the period of imitation smoking. It is therefore due to the action of substances in the tobacco smoke.

It is possible, therefore, that the discrepancy between our results and those of other workers may be explained by a difference in the rate of smoking adopted. Maddock and Coller (1933) stated that their subjects were given their customary form of tobacco to smoke at their normal rates, but occasionally a subject noted mild vertigo and nausea on smoking. Wright and Moffat's (1934) subjects, who were experienced smokers, also were urged to smoke at their normal rate, though they state that it is probable that there was an increase in both the rate and the depth of inhalation during the experiment. In some of their subjects severe symptoms developed during smoking, including "nausea with vomiting, marked vertigo, cold sweats, pallor, and even profound syncope."

None of our subjects experienced any unpleasant symptoms while inhaling at minute intervals, and, although the rate of smoking is not given by the workers mentioned, it seems likely from the symptoms described that it was more rapid than normal.

Roth, McDonald, and Sheard (1944), who found a very marked decrease in the skin temperature of the extremities with smoking, also state that their subjects inhaled with their accustomed depth and frequency, though they also do not say what this was. They state, however, that their subjects fasted for 15 hours and then smoked two cigarettes in succession until two-thirds of each had been smoked. The smoking period generally lasted 12–16 minutes. They found larger increases in pulse rate and blood pressure during smoking than we obtained on our subjects when inhaling with British or American cigarettes at 20-second intervals. When two of our subjects inhaled at this rate, however, following a 15-hour period without food and cigarettes, increases in pulse rate and blood pressure were observed similar to those described by Roth *et al.*

Summary

The frequency of inhalation of tobacco smoke has been determined in 50 male subjects. The average time between inhalations was 66 seconds.

Simultaneous measurements of hand blood flow and stethographic records of the respiratory movements have been made in moderate cigarette-smokers during smoking and imitation smoking.

Inhalation of the tobacco smoke at intervals of a minute (approximately the normal rate) leads to a transient decrease in flow at the moment of inhalation. A similar decrease occurs when inhalations of the same depth are carried out with the cigarette unlit.

The transient decrease in flow is therefore due to the physiological effect of the deep breath associated with the inhalation, and not to the pharmacological action of substances in the tobacco.

Apart from this decrease in flow on inhalation, the general level of hand blood flow is unaltered during and immediately after smoking one cigarette at this rate.

When cigarette smoke is inhaled every 20 seconds—that is, more rapidly than normal—the hand blood flow steadily decreases during the smoking period. There is no decrease in the general blood-flow level when inhalations of similar depth are made with the cigarette unlit.

When cigarettes are smoked at a rate in excess of the normal the resulting decrease in hand blood flow is therefore mainly pharmacological and not physiological in origin.

The significance of previous work on smoking where the frequency of inhalation has not been controlled or is not stated is therefore difficult to assess.

My thanks are due to Dr. C. de Largy for his collaboration in the earlier experiments. I would also thank my colleagues and students who acted as subjects.

References

Barcroft, H., and Edholm, O. G. (1945). *J. Physiol.*, **104**, 161.
Bolton, B., Carmichael, E. A., and Stürup, G. (1936). Ibid., **86**, 83.
Brodie, T. G., and Russell, A. E. (1905). Ibid., **32**, XLVIIP.
Gilliatt, R. W. (1948). Ibid., **107**, 76.
Hewlett, A. W., and Van Zwaluwenburg, J. G. (1909). *Heart*, **1**, 87.
Lampson, R. S. (1935). *J. Amer. med. Ass.*, **104**, 1963.
Maddock, W. G., and Coller, F. A. (1933). *Ann. Surg.*, **98**, 70.
Mulinos, M. G., and Shulman, I. (1940). *Amer. J. med. Sci.*, **199**, 708.
Roddie, I. C. (1951). *J. Physiol.*, **112**, 204.
Roth, G. M., McDonald, J. B., and Sheard, C. (1944). *J. Amer. med. Ass.*, **125**, 761.
Wright, I. S., and Moffat, D. (1934). Ibid., **103**, 318.

TOXAEMIA OF PREGNANCY

SOME EPIDEMIOLOGICAL RELATIONSHIPS TO NEPHRITIS, RHEUMATIC FEVER, AND STILLBIRTH

BY

T. W. BUCHAN, M.B., F.R.F.P.S., D.P.H.

A recent study of the effect of cortisone in toxaemia of pregnancy (Moore *et al.*, 1951) suggests that this condition is related to rheumatic fever and nephritis, and it is of interest to explore the possible relationship by investigating the regional distribution of the maladies concerned by making use of the relevant mortality statistics as provided by the Registrar-General of England and Wales. Stillbirth is a related problem, a proportion of stillbirths being directly attributable to eclamptic and nephritic toxaemia. Data on this aspect are therefore included in the present study.

Regional Variations

In a previous paper (Buchan, 1950a) the closely analogous distribution of eclampsia and stillbirth was noted. Our concern now is with the regional variations of rheumatic fever, acute nephritis, scarlet fever, puerperal sepsis, stillbirth, and eclampsia. There is considerable evidence that rheumatic fever and acute nephritis represent an allergic response to invasion by a haemolytic streptococcus, and it is convenient to begin the present study by inquiring whether mortality from these two diseases shows any correspondence in regional distribution.

Their mortality in England and Wales cannot be directly investigated because before 1940 deaths were not tabulated under these headings on a regional basis in the Registrar-General's *Statistical Review*. Even in 1940 and subsequent years, of these two diseases, deaths from rheumatic fever alone are so classified, and then not in age groups, so only crude rates can be calculated. Crude rates, however, are not satisfactory indices of mortality on account of the differing age constitution of the relevant populations, but in seeking to investigate the regional distribution of rheumatic fever there are good reasons for using as indices the death rates in the younger age groups from the causes included under the broad heading of "heart diseases." Knowelden (1949) shows that in the 5–14 age group over 90% of the deaths under this large heading are almost entirely rheumatic in origin, and in the 15–24 age group, 86%; accordingly, it is reasonable to use such age-group death rates as indices of mortality from rheumatic fever. Similar data are available under the heading of "nephritis."

Tabulation of the deaths for the years 1932–7 shows that at ages 5–14 years 46% of deaths debited to this cause fell to the title "acute nephritis," and at ages 15–24 years 27% were so classified. Of those falling to chronic nephritis, the corresponding figures were 43% and 53%, but it is reasonable to assume that, in these age groups, deaths so assigned were almost all secondary to acute nephritis. The death rates under nephritis in these two age groups may therefore be taken as valid indices of mortality from acute nephritis.

The death rates for the years 1932–7 for heart disease and nephritis respectively in those two age groups in each of the twelve main regions of England and Wales are contained in Table I. The coefficients of correlation between the rates for the two diseases in the same age groups are also given (Table II). The coefficient between

TABLE I.—*Regional Death Rates in 1932-7 in England and Wales*

Region*	Per Million Living					Per 1,000 Total Births		Per Million Living
	Heart Disease		Nephritis		Scarlet Fever	Puerperal Sepsis	Stillbirth	Cancer†
	5–14 Years	15–24 Years	5–14 Years	15–24 Years	0–4 Years			15–24 Years
	1	2	3	4	5	6	7	8
Greater London	102	189	28·5	60·2	83	1·27	32	44
Remainder of S.E.	60	121	25·1	44·0	54	1·37	35	43
North I	121	252	46·4	77·6	264	1·89	42	41
North II	116	224	31·1	61·5	74	1·75	42	45
North III	130	252	38·4	82·5	135	1·79	46	44
North IV	136	254	39·5	80·1	94	1·52	46	43
Midland I	101	218	33·1	75·0	70	1·61	40	52
Midland II	101	195	34·5	80·1	54	1·53	41	40
East	59	127	21·3	57·8	31	1·38	38	41
South-west	65	113	31·6	44·8	40	1·26	40	45
Wales I	167	335	50·6	95·2	114	2·13	55	36
Wales II	95	199	31·6	93·3	76	1·77	52	42

* For the geographical constitution of the regions, see the Registrar-General's *Statistical Review*, any recent issue.

† These rates are included as a check. They do not show a significant degree of correlation with any of the other rates.

TABLE II.—*Correlation Coefficients of Regional Death Rates in Table I*

r13 = +0·87 HS	r24 = +0·80 HS	r35 = +0·71 HS	r45 = +0·41 NS	r56 = +0·65 S	r67 = +0·80 HS
r15 = +0·54 NS	r25 = +0·58 S	r36 = +0·74 HS	r46 = +0·73 HS	r57 = +0·60 S	
r16 = +0·74 HS	r26 = +0·82 HS	r37 = +0·67 S	r47 = +0·81 HS		
r17 = +0·66 S	r27 = +0·69 S				

The first two numbers refer to columns in Table I—for example, r13 means coefficient of correlation of columns 1 and 3. HS = Highly significant, implying a chance probability less than 0·01. NS = Not significant, implying a chance probability greater than 0·05. S = Significant, implying a chance probability between these values.

the two series of rates in the 5–14 year age group is +0.87 and in the 15–24 year age group it is +0.80. These values are highly significant and provide evidence of a direct relationship between the regional distribution of mortality from rheumatic fever and acute nephritis.

Some Comparisons

The regional variations of rheumatic fever and acute nephritis may now be compared with those of the two streptococcal infections chosen, scarlet fever and puerperal sepsis (Tables I and II). With the use of the first of the two indices for rheumatic fever—namely, heart disease mortality at 5–14 years—the correlation (+0.54) with the scarlet fever death rates at 0–4 years is just short of the arbitrary level of statistical significance. With use of the second index (heart disease mortality at 15–24 years) the coefficient is +0.58, and is significant. Taking now the nephritis rates, we find that in the 5–14 age group the correlation (+0.71) with scarlet fever is highly significant, but in the 15–24 age group for nephritis it is not significant though it is suggestive (r = +0.41). These results are in harmony with the known clinical relationship between scarlet fever and both rheumatic fever and acute nephritis. The puerperal sepsis values show a close correspondence with those of rheumatic fever and acute nephritis, all the coefficients being of the "highly significant" level. This rather striking

result would seem to extend to a wider field the accepted relationship of rheumatic fever and acute nephritis to streptococcal infection. The correlations between rheumatic fever and stillbirth, and between acute nephritis and stillbirth, are all significant or highly significant. Moreover, the correlation of puerperal sepsis and stillbirth gives a highly significant coefficient (+0.80), which is greater than that previously shown between eclampsia and stillbirth (r= +0.77).

In Table III the regional death rates for nephritis in 1932–41 are given. These are average rates—that is to say, arithmetic means of the rates at 0–4, 5–14, and 15–44 years. Mortality from eclampsia is represented by the average annual rates calculated from deaths assigned to the puerperal toxaemias in the years 1939–46. The difference in the two periods of years, which is of little consequence, arises from the fact that relevant data of the same periods are not at hand. In the correlation of these two columns r= +0.71, a highly significant figure. The coefficient between puerperal sepsis (1932–7) and eclampsia (1939–46) is +0.61, and is significant.

TABLE III.—*Regional Death Rates in England and Wales*

Region	Nephritis 0–44 Years per Million Living, 1932–41	Eclampsia per 1,000 Live Births and Stillbirths, 1939–46
	1	2
Greater London	49·2	0·42
Remainder of S.E.	44·0	0·54
North I	73·9	0·64
North II	57·0	0·60
North III	65·9	0·55
North IV	68·5	0·55
Midland I	61·3	0·56
Midland II	59·9	0·55
East	43·8	0·52
South-west	53·8	0·68
Wales I	80·4	0·77
Wales II	77·6	0·82

Coefficient of correlation of columns 1 and 2 = +0·71. Coefficient of correlation of column 2 and column 6 of Table I = +0·61.

The association of high rheumatic fever and nephritis rates with high mortality from the streptococcal infections coincides with the seasonal experience of these conditions (Buchan, 1950b) and might have been expected, but the broad correspondences between stillbirth and rheumatic fever, nephritis, scarlet fever, and puerperal sepsis appear to raise the question of the relationship of streptococcal infection to stillbirth. Are unexplained stillbirths the effect, like rheumatic fever, of a factor associated with susceptibility to streptococcal infection? Here is a problem intertwined with social and environmental complexities of which the present limited analysis takes no account. But the general picture suggests, though it does not prove, that streptococcal infection plays a part in eclampsia and stillbirth—an aspect which seems worthy of further research.

Summary

In view of the possible relationship between eclampsia and both acute nephritis and rheumatic fever, the regional distribution in England and Wales of mortality from these diseases and from scarlet fever, puerperal sepsis, and stillbirth is considered.

Eclampsia and stillbirth have a similar regional distribution and are in frequent association clinically.

If heart disease mortality at 5–14 and 15–24 years is used as an index of rheumatic fever, and nephritis mortality in the same age groups as an index of acute nephritis, a close correspondence between the regional distribution of these two diseases is revealed.

The values for rheumatic fever and acute nephritis correlate fairly well with the scarlet fever death rates at 0–4 years, and a direct relationship of rheumatic fever and acute nephritis with puerperal sepsis is clearly indicated. The coefficients between rheumatic fever mortality and stillbirth and between acute nephritis mortality and stillbirth are significant or highly significant. Puerperal sepsis is closely correlated with stillbirth, a result which points to the need for further inquiry into this aspect of the problem of stillbirth.

A close correspondence also exists between the regional variations of mortality from eclampsia, from nephritis, and from puerperal sepsis, a circumstance which, along with the other relationships indicated, would seem to support the use of cortisone in toxaemia of pregnancy, as well as in other diseases suspected of being streptococcal allergic disorders.

REFERENCES

Buchan, T. W. (1950a). *British Medical Journal*, **2**, 22.
—— (1950b). Ibid., **1**, 1268.
Knowelden, J. (1949). *Brit. J. soc. Med.*, **3**, 29.
Moore, H., *et al.* (1951). *British Medical Journal*, **1**, 841.

Medical Memorandum

Total Gastric Polyposis With Malignant Changes

In the routine clinical practice of a general hospital gastric polyposis is encountered somewhat infrequently, but assumes importance by virtue of the twin complications of malignancy and recurrent haemorrhage.

Menetrier (1888) was among the earlier observers to comment on the tendency to malignant change, but it was Quain (1857) who placed on record the first instance in which the diagnosis was made during life, in the case of a girl of 19, by the presence of a tumour the size of a chestnut in the patient's vomit.

The rarity of the condition may be appreciated from the findings of two series of necropsies: in the one, Stewart (1929) at Leeds noted 47 cases of gastric polyposis in a study of 11,000 cases (0.43%); while in the second, Lawrence (1936), at the Cook County Hospital, U.S.A., observed 50 in 7,000 examinations (0.71%).

The frequency of malignant change recorded by different observers may be seen by reference to the accompanying Table. In terms of age and sex, the incidence of gastric polyposis is greater in males above 50 years of age, in the proportion of 9 to 4 (Lawrence, 1936) or 2 to 1 (Chamberlin, 1938).

Author	Year	Cases of Gastric Polyposis	Malignancy %
Brunn and Pearl	1943	41*	51·0
Lawrence	1936	50	18·0
Benedict and Allen	1934	17	41·2
Miller, Eliason, and Wright	1930	23	35·0
Stewart	1929	47	28·0
Balfour and Henderson	1927	57	3·5
Brunn and Pearl	1926	84	12·0
Mills	1922–3	19	20·0

* Includes four cases in which data regarding malignancy were lacking.

Symptoms are not as a rule typical, and may be absent if the polypi are situated away from the pylorus (Spriggs, 1942). When present, epigastric pain and vomiting in relation to meals may be conspicuous, due to the prolapse of polypi through the pylorus with sequential intermittent obstruction. Anorexia is common, usually in association with achlorhydria, whose constancy has

been stressed by several observers. However, above the age of 50 years asymptomatic achlorhydria is a not infrequent finding, and has been recorded in 35% of individuals over the age of 60 (Vanzant *et al.*, 1932).

A unique feature is the presence of portions of polypi in the vomit, as observed in the case reported here. Constitutional symptoms such as weakness are the consequence of continued bleeding from the site of ulceration of the polypi.

Radiological investigation may prove diagnostic if multiple pea-sized filling defects of regular outline are demonstrated on the greater curvature, in the presence of normal mobility and tonus of the stomach. Such a typical appearance has been described as that of a "bag filled with beans."

Case Report

A girl aged 19 complained that for a twelvemonth she had felt a dull ache in the abdomen immediately after meals, unrelieved by alkalis. There were no remissions. In the past month, in addition to loss of appetite and irregular bouts of vomiting, she had found it a commonplace to awaken shortly after midnight on account of pain, and had obtained relief from a meal of gruel. Her weight was stationary. The psychological background did not provide any data which might give an explanation of the symptoms. The past history was without significance.

Clinically, the general nutrition was good and the dental state excellent. On examination a slight degree of guarding was detected in the epigastrium to the left of the midline; no organ or mass was palpable, and the "sentinel gland" in the left supraclavicular fossa could not be felt. Rectal examination revealed no melaena or other abnormality.

It was considered probable that an organic lesion would account for the periodicity of the symptoms, in particular nocturnal epigastric pain, but the good state of nutrition and the failure to respond to alkalis militated against the obvious diagnosis of peptic ulceration.

Investigations

Blood Count.—Red cells, 4,600,000 per c.mm.; Hb, 10.6 g. per 100 ml.; white cells, 8,400 per c.mm. (N. 64%, L. 30%, M. 4%, E. 1%, B. 1%).

Fractional Test-meal.—Resting-juice volume, 24 ml.; histamine-fast achlorhydria on two occasions; no blood present.

Occult Blood in Stools.—Variable, usually a trace.

Barium-meal Studies.—First report as follows: "Body of stomach normal. Some mobile filling defects in the antrum—almost certainly food residue. Deformed duodenal cap—ulcer. Four hours after food: one-quarter residue in the stomach." Second report, one month later: "There is still a marked prepyloric filling deformity, and the pyloric antrum was at no time seen to fill regularly—no local tenderness. In spite of this patient's age, and in view of the achlorhydria, a prepyloric neoplasm certainly cannot be excluded. Four hours after food—stomach almost empty." Third report, after a further month: "Still an extensive filling defect in the pyloric antrum, which must be regarded as carcinoma until proved otherwise. Four hours after food—stomach empty." (Dr. J. C. Bishop.)

Gastroscopy was contemplated at this stage, but before it was carried out the patient had a bout of vomiting which produced a small solid round mass, the size of a cherry-stone, which she described as a "piece of flesh." That this specimen was a portion of a polypus was now evident, and histologically it represented a papilloma with the additional feature of mitosis in many of the cell groups. (Dr. G. C. Reid.)

Gastroscopy.—(By Dr. C. R. St. Johnston.) This disclosed diffuse polyposis of the stomach from the pylorus to within a few centimetres of the cardia. Over the greater curvature and anterior wall the polypi were most extensive; at one place on the anterior wall a pedunculated polyp was seen hanging from the cardia, its apex being necrotic and blood-stained. From the lesser curve the appearance simulated "stalactites." At the pylorus a rounded polyp the size of a marble was clearly discerned.

These features were considered to indicate that malignant changes were present, and total gastrectomy was advised. A further radiological investigation of the gastro-intestinal tract prior to operation showed no evidence of polypi in the remainder of the bowel.

Operation.—(Initially by Mr. R. Forrest and later by Mr. Scott Mason.) The stomach was found to be thickened by involvement of the peritoneal coat with carcinoma. Enlarged glands were present along the lesser curve and the upper border of the pancreas. An attempt at separation failed owing to the existence of adhesions between the stomach and the liver, diaphragm, and spleen. In the circumstances, any palliative procedure was technically impossible, and the abdomen was closed. The patient died a few weeks later.

Comment

In the investigation of abdominal symptoms in young adults the finding of histamine-fast achlorhydria may be of sinister significance, and merits gastroscopic examination to determine whether polyposis is present. Such visual examination will not disclose the presence of malignant changes—for which histology is the only certain method—but the extent and appearance of the polypi will be demonstrated.

If extensive, radical surgery is the treatment of choice at an early date, in the light of the statistics reflecting the frequency of malignant metaplasia.

My thanks are due to Dr. S. C. Dyke, in whose care this patient was admitted to the Medical Unit at Walsall, and to Mr. R. P. Scott Mason, of the Queen Elizabeth Hospital, Birmingham, for the operative findings.

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References

Balfour, D. C., and Henderson, E. F. (1927). *Ann. Surg.*, **85**, 354.
Benedict, E. B., and Allen, A. W. (1934). *Surg. Gynec. Obstet.*, **58**, 79.
Brunn, H., and Pearl, F. (1926). Ibid., **43**, 559.
—— —— (1943). Ibid., **76**, 257.
Chamberlin, D. T. (1938). *Surg. Clin. N. Amer.*, **18**, 649.
Lawrence, J. C. (1936). *Amer. J Surg.*, **31**, 499.
Mallory, T. B. (1939). *New Engl. J. Med.*, **220**, 480.
Menetrier, P. (1888). *Arch. Physiol. norm. path.*, **1**, 32, 236.
Miller, T. G., Eliason, E. L., and Wright, V. W. M. (1930). *Arch. intern. Med.*, **46**, 841.
Mills, G. P. (1922–3). *Brit. J. Surg.*, **10**, 226.
Quain, R. (1857). *Trans. Path. Soc.*, **8**, 219.
Spriggs, E. I. (1942). *Quart. J. Med.*, n.s. **12**, 1.
Stewart, M. J. (1929). *British Medical Journal*, **2**, 567.
Vanzant, F. R., *et al.* (1932). *Arch. intern. Med.*, **49**, 345.

In his annual report for 1950 Dr. C. Metcalfe Brown, the medical officer of health for Manchester, describes the results of a survey into the incidence of mental deficiency and mental illness in each ward of the city. For mental deficiency there was a recorded incidence of 3.24 per 1,000 of the population. Accurate figures of mental illness are of course difficult to obtain, but an estimate based on hospital admissions of voluntary, temporary, and certified patients gave an incidence of 3.41 per 1,000. There was more mental deficiency and mental ill-health in the older and more populated districts than in other parts of the city.

Reviews

STRESS

The Physiology and Pathology of Exposure to Stress. A Treatise based on the Concepts of the General-Adaptation-Syndrome and the Diseases of Adaptation. By Hans Selye, M.D., Ph.D.(Prague), D.Sc.(McGill), F.R.S.(Canada). (Pp. 1,025; illustrated. No price.) Montreal, Canada: Acta-Endocrinologica Inc. 1950.

The main outline of the text of this book on stress must be well known to British workers interested in this field through Professor Selye's many previous publications and through the Heberden Oration and other lectures that he gave in England last year. His views on the effects of stress have been set out in detail. It is a large book—822 pages of text including a 30-page index, accompanied by an extensive bibliography of over 5,500 references (given with titles) that occupy about another 200 pages.

After a short historical introduction the author discusses the general concept of adaptation to stress (Selye's "general-adaptation-syndrome," G.A.S.), the various types of stress stimuli, and resistance to stress and the factors which influence this resistance. In the greater part of the book he describes the effects of stress on the different systems of the body—metabolic, endocrine, skeletal, haemopoietic, lymphatic, cardiovascular, renal, respiratory, muscular, nervous, sensory, gastro-intestinal, hepatic, salivary glands, and so on. He reviews the effects of different types of stress on the particular system and then the factors which modify these responses to stress; finally he makes suggestions on clinical conditions which might arise through abnormal responses to stress. On page 772 the author remarks, "Up to the month of May, nineteen hundred and fifty, this is all I have learned, that deserves to be recounted, about the General-Adaptation-Syndrome and the Diseases of Adaptation." A twenty-page summary concludes the book—a summary which might be read with advantage as part of the introduction as well as the conclusion.

This book is clearly of a personal nature. As is well known, Professor Selye has contributed much original work on the physiology of stress responses (there are 188 references to papers by himself and his group in the bibliography). In view of the recent clinical findings regarding A.C.T.H. and cortisone therapy he has presented here a survey of his own work and theories, together with a mass of related data from the literature, in an attempt to produce a coherent, unified system of thought on stress responses and the diseases that may arise therefrom. He suggests that all forms of stress, whether trauma, haemorrhage, burns, exposure to extremes of environmental temperature, emotional stimuli, muscular exercise, asphyxia, infections, and so on, elicit the same general adaptive responses on the part of the body, the "general-adaptation-syndrome." This general syndrome occurs in three stages—the alarm stage, the stage of resistance, and the stage of exhaustion—the changes being co-ordinated through the hypothalamus acting via the autonomic nervous system and via the pituitary and other endocrine glands. According to various conditioning factors (heredity, diet, pre-existing disease of various organs, previous exposure to stress, etc.), so the adaptive responses of the body may vary, and the G.A.S. may manifest itself in widely differing ways. Disorders of the adaptive processes (in which the adrenal cortex appears to play a prominent role) may result in disease, the "diseases of adaptation." In this way he reasons that rheumatoid arthritis, periarteritis nodosa, allergies, certain types of diabetes, hypertension, and other conditions are all due to the same causative agent—namely, to systemic stress.

Much in the book is controversial. This is necessarily so with regard to the new ideas and theories presented, for, as stated in the foreword, "the value of a scientific theory does not depend as much on its correctness as upon its fertility. . . ." From this point of view Professor Selye has rendered a valuable service in collecting and reviewing the data and in presenting the whole in such a stimulating form. There is no doubt that the ideas put forward will do much to excite further work, and for this reason, as well as for the extensive bibliography quoted, the book will be of much value to every investigator interested in stress or in the adrenal glands. It might be suggested that the value of a book of this size, dealing with subjects that progress so rapidly as the physiology of stress and the adrenal cortex, is partially lost because much in it needs revision and modification within a short time. For example, Selye in a recent paper (*British Medical Journal*, February 10, p, 263) has produced evidence that what he describes in the book as the "X principle" is in reality the somatotrophic or growth hormone. In this respect it is reassuring that there are plans for producing a yearly compendium ("Annual Report on Stress," Acta Inc., Montreal) under Professor Selye's editorship, dealing with future work on this subject. The general production of the book is excellent. The binding, paper, print, and plates leave little to be desired.

G. W. HARRIS

PARENTCRAFT

The Teaching of Parentcraft. By Leslie George Housden, O.B.E., M.D. (Pp. 140. 7s. 6d.) London: Methuen and Co. 1951.

The author intends his book for those who have some practical concern with instruction in parentcraft, especially during the years of compulsory education. But it will not tell them in any detail how to teach the subject. A better title for the book would be "What to Teach as Parentcraft," and it has unity only if classed among essays delimiting a subject.

Naturally, the care of children is central; and the author divides this branch of the subject into the guidance of children as personalities and the care of children as animals. He would also include under parentcraft the entire subject of domestic economy—though this is not applicable to parents alone. He would include the art of living in harmony as husband and wife, and some other aspects of marriage guidance, but not sex education or birth control. He would have it emphasized throughout all the teaching that the object of parentcraft is to increase the joy of living for all members of the family community, but he does not specifically include either adult psychology or any system of ethics. Religion is to preside remotely over all. This description of the subject fills about two-thirds of the book, and leaves the present reviewer with the feeling that parentcraft is exceedingly difficult to define, but that even so the author's limits are arbitrary.

The last part of the book consists of extracts from essays submitted by health visitors and midwives, by mothers, and by schoolgirls aged between 14 and 18 for prizes offered by the National Baby Welfare Council.

The author quotes them as though they represented the opinions of the writers; but there is much to suggest that they contain merely the opinions which the writers thought likely to win prizes. In consequence a feeling of unreality pervades these later chapters.

F. CHARLOTTE NAISH.

DIABETES AND THE LIVER

Le Foie Diabétique. Aspects Hormonaux. By Dr. Jacques Mirouze. (Pp. 368. 1,300 francs.) Paris: L'Expansion Scientifique Française. 1951.

This book on the "diabetic liver" is difficult to review. To size up and assess detailed and specialized monographs in the French mode of production, and indeed in special supplements of the *Acta Scandinavica*, often leaves the mind of an English reviewer full of headache and confusion. He may appreciate the linguistic clarity of every sentence, but must wonder what all the details in each chapter and section want to say or prove. Even the final summary and conclusions are too often pervaded with a vagueness and verbosity at which the Anglo-Saxon mind revolts—or so has mine when I have tried to comprehend the purport of these 368 pages.

The book is primarily concerned with the liver in different forms of diabetes. In the first section the author describes—mainly from the literature—different types of experimental and human diabetes. In the second section he describes human investigations of liver function in diabetics for the study of blood, pigment, and protein, fat, and glycogen metabolism, based principally on liver biopsies. When one looks for numbers tested and precise description of techniques, a soft vagueness pervades. When we turn to the general conclusions of this book, we learn that no strict, and certainly no causal, relation is obvious between diabetes and the liver changes that may be found in diabetics.

R. D. LAWRENCE.

CANCER OF THE BLADDER

Cystektomie beim Blasenkrebs. By Professor H. Boeminghaus. (Pp. 84; 56 illustrations. M. 11.50.) Stuttgart: Georg Thieme. 1951.

Twenty years ago there were few forms of malignant disease regarded with such despair as that of the bladder. Radical operation involved a risk which was almost prohibitive, and even alleviation of the terrible distress of the patient was often impossible. To-day, with modern resources, a total cystectomy may be achieved with no more risk than that of a resection of the colon, and there is a reasonable prospect of years of normal life.

This book on cystectomy for cancer of the bladder gives an excellent account of the present position. Although the personal experience of the author is limited, he has evidently studied the literature very thoroughly. His discussion of the indications for and against total cystectomy is admirable, and he makes clear the advantages of a complete over a partial operation. The description of this considerable operation as carried out by the leading authorities is sound and is fully illustrated from their own articles, chiefly from the work of Millin and Couvelaire. A bibliography would have been welcome, but this could easily be supplied from the full lists of names which accompany the statistical tables.

To anyone with a knowledge of German this monograph gives valuable information in a convenient and reliable form, and it will enable him to appreciate the extraordinary advance made in the surgery of malignant disease of the bladder in recent years.

HENRY SOUTTAR.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received

Patterns of Marriage. By E. Slater, M.A., M.D., F.R.C.P., and M. Woodside. (Pp. 311. 17s. 6d.) London: Cassell. 1951.

Wonderfully Made. By A. R. Short, M.D., F.R.C.S. (Pp. 159. 6s.) London: The Paternoster Press. 1951.

The Midwife's Text-Book. By R. W. Johnstone, C.B.E., M.A., M.D., LL.D., F.R.C.S.Ed., M.R.C.P.Ed., F.R.C.O.G., F.R.S.Ed. 5th ed. revised in collaboration with W. I. C. Morris, M.B., F.R.C.S.Ed., F.R.C.O.G. (Pp. 400. 20s.) London: Adam and Charles Black. 1951.

Medical Care for Seamen. By Professor R. Straus. (Pp. 165. 24s.) London: Geoffrey Cumberlege. 1950.

Spleen Puncture. By S. Moeschlin; translated by A. Piney, M.D. (Pp. 229. 30s.) London: William Heinemann. 1951.

A Synopsis of Regional Anatomy. By T. B. Johnston, C.B.E., M.D. 7th ed. (Pp. 448. 22s. 6d.) London: J. and A. Churchill. 1951.

The Child Who Never Grew. By Pearl S. Buck. (Pp. 60. 2s. 6d.) London: Methuen. 1951.

Epitome of the Pharmacopeia of the United States and the National Formulary. By the Council on Pharmacy and Chemistry of the American Medical Association. 9th ed. (Pp. 255. 20s.) London: J. B. Lippincott. 1951.

Introduction to Surgery. By V. K. Frantz, M.D., and H. D. Harvey, M.D. 2nd ed. (Pp. 233. 21s.) London: Geoffrey Cumberlege. 1951.

An International Bibliography on Atomic Energy. Vol. 2: Scientific Aspects. By the Atomic Energy Commission Group. (24,282 items. 75s.) London: H.M.S.O., P.O. Box 569, S.E.1. 1951.

The Human Colon. By W. J. Grace, M.D., and others. (Pp. 239. $7.50.) New York: Paul Hoeber. 1951.

Manual of Tumor Nomenclature and Coding. Prepared by Subcommittee of the Statistics Committee, American Cancer Society. (Pp. 119. $2.50.) New York: American Cancer Society. 1951.

Atlas der Hals-Nasen-Ohren-Krankheiten. By Professor C. von Eicken and A. S. van Treeck. 3rd ed. (Pp. 199. M. 78.) Stuttgart: Georg Thieme. 1951.

Atonies et Dyskinésies Digestives: Colites Chroniques et Ptoses. By L. Gleize-Rambal. (Pp. 81. No price.) Paris: G. Doin. 1947.

Unsurpassed as a medical dictionary, *Dorland's* maintains its high standard in the twenty-second edition, recently published by W. B. Saunders at 50s. It includes a new introductory article by Professor Lloyd W. Daly, of Pennsylvania University, on "Fundamentals of Medical Etymology." Here Latin and Greek are anatomized to show how their vocabularies have been drawn upon in the construction of medical and scientific terminology. The dictionary has been brought up to date by the addition of many new terms, though at the same time an attempt has been made to keep as many as possible of the old ones. The book is thus something more than a dictionary of current terminology, being also a fascinating museum and including brief biographical notes of the many men whose names are commonly attached to diseases, signs, symptoms, and tests. There are also useful tables of drug doses and weights and measures. The text has been reset in a new type which makes the page easier to read.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY OCTOBER 27 1951

FIFTY YEARS OF PAEDIATRICS

The October issue of the *Archives of Disease in Childhood* is published in honour of Sir Robert Hutchison on the occasion of his 80th birthday. Numerous old pupils, most of whom have served him as house-physicians either at the London Hospital or at The Hospital for Sick Children, Great Ormond Street, have contributed to this issue. Their affection and regard is but a sample of that held by hundreds who have served or read or listened to a great master.

It is over 50 years since Sir Robert was elected to the staff at Great Ormond Street, and this period has seen remarkable changes in the field of paediatrics. In 1900 Sir Frederic Still was almost alone in Great Britain in restricting his hospital and private work to children. To-day there are few paediatricians who also serve as general physicians. The obvious reason for this change, often perhaps wrongly called an increase in specialization, is the increasing complexity of medicine. The days have gone when a fairly firm diagnosis could be reached by a process of careful history-taking and physical examination, aided by a long experience and followed by a carefully worded prognosis. Aids to diagnosis—radiological, chemical, microscopical, and electrical—imply a technical skill which obviously varies in kind according to its application to a young infant or an adult. Moreover, the technical advances in treatment mean a long apprenticeship in the children's hospital by residents and registrars. To become to-day an all-round general physician for all ages of patients is probably beyond the resources, financial and even intellectual, of most consultants in training. A similar process is to some extent seen in the breaking-off from the general field of neurologists, heart specialists, dermatologists, and chest physicians. Yet this type of specialization is fortunately not seen to any extent in paediatrics.

Paradoxically, as befits a branch in which the demarcation is based on age instead of regional or system involvement, paediatrics—defined as general medicine in the younger age groups—has remained or even become more comprehensive as general medicine has shrunk and become more specialized. The paediatrician must be able to examine and reach a firm opinion upon the eyes, ear drums, and central nervous system of his patients without calling in the experts save for the unusual and rare. He must deal with the common skin disorders. He must have a wide knowledge of the psychology of childhood and of adults in so far as they are concerned with children, whether as parents or as attendants upon the sick or well child. He must be able to estimate the mental state of babies and older children. Nor is he confined to the usual province of a physician. He must be sufficiently trained in surgery to be able to diagnose and select for treatment most of the orthopaedic disorders of early life. It is the children's physician rather than a surgeon who is the first specialist usually called to see the child with an acute abdominal catastrophe. If the paediatrician is serving in a maternity unit he must be familiar with the problems of obstetrics, keeping himself up to date in matters of obstetrical treatment, including analgesic and anaesthetic agents, in order that he may discuss these matters with his obstetric colleagues. In the puerperium he may have to collaborate closely if troubles arise in connexion with the appropriately called no-man's-land of the mammary gland. Indeed, the paediatrician is nearer to being a general practitioner than any of his specialist colleagues.

It is not only in the field of disease that these 50 years have seen great changes in paediatrics. In the preventive services the growth of infant welfare and of school health has been equally remarkable. The most promising fields of prevention have been found in the ages served by paediatrics, and although there was a period between the two wars when the two main divisions of medical work for children—curative and preventive—were drifting further and further apart this tendency has now been happily reversed. With chairs of child health established at all the universities of Great Britain and Northern Ireland except Oxford and Cambridge, there is not only academic recognition of the importance of the subject but in the very title of such chairs an emphasis on the preventive side which is of great importance. The increasing interchange of medical officers between the staffs of hospitals and local health authorities is another satisfactory aspect of the modern trend.

Some of the contributions in the *Archives* indicate a striking change in the picture and incidence of disease. Surgical refinements in the treatment of tuberculous meningitis (Professor Sir Hugh Cairns) can now be discussed, when only recently there was

not even a drug which did any good. The changes noted in the mortality of young children in Aberdeen (Professor John Craig) can be matched throughout the country. Indeed, even in the comparatively short time since Sir Robert ceased to be on the active staff at The Hospital for Sick Children, revolution is not too strong a word for the changes there, principally changes which reflect the effects seen throughout the medical world of modern chemotherapy and the antibiotics. As a keen and expert therapeutist Sir Robert would have enjoyed the past 10 years even while regretting the passing of the elegant prescription. The modern simplification of infant feeding owes much to his teaching. His pupils in responsible positions to-day probably quote him directly or indirectly more than anybody else. Thus his influence over the developments of this half-century in paediatrics has been profound. Of some he would probably sternly disapprove, but of most he can rightly be proud, for he had a large share in the building of the British school of paediatrics, which can hold its pre-eminent place to-day with confidence in the future.

PROFESSION AND STATE

When the profession entered the Health Service in 1948 it did so only after it had secured safeguards against certain dangers likely to threaten the free and personal practice of medicine, and in the expectation that professional liberty would not be seriously imperilled. Many doctors entered it with reluctance and apprehension, feeling rather that they had been clapped into uniform while accepting assurances that skilled tailors would immediately get down to the task of making it fit in accordance with professional and public needs. Some reforms have been achieved, but too few. The Government has here and there gone some way towards meeting the profession's wishes, but often not far enough; and many of the concessions have been made on small administrative details only after almost interminable parleys. One of the outstanding reasons for all this—and it was as plain at the 1950 general election as it is now—is that political parties regard the Health Service as a valuable asset on political platforms. Claims and counter-claims on the origin, structure, and benefits of the N.H.S. are put before the electorate—of whom an annoying minority have used the Service not wisely but too well. While the Service is treated in this way, doctors must feel painfully anxious about their relations with whatever Government is in power.

We went to press before the results of the general election were known, but, as many have emphasized, the Health Service must be freed from party politics. This is not impossible. The urgent need for a new attitude to the problem is revealed by that part of the B.M.A. Council's recent report[1] which is concerned with arbitration and, by implication, with a relationship between profession and State which gravely affects professional freedom. The main features of the present position are, first, that the profession is powerless to compel any dispute to be taken to arbitration if agreement cannot be attained, and, secondly, that a Minister can set aside any decision attained by arbitration. The constitution of the Health Service Whitley machinery makes provision for an arbitration agreement, but agreement has not been achieved. This is because the management side, representing Government and other employing bodies, has never conceded the demand of the staff side, representing employees in the Health Service, that either side may take a dispute to arbitration without the consent of the other and have the decision enforced. So long as the profession is held powerless in this way by the State it will be permeated by that feeling of frustration and dissatisfaction which we referred to a fortnight ago.[2] In addition Dr. Gorsky has drawn attention[3] to a dangerous possibility arising under S.I. 1376. This enables the Minister of Health or a hospital authority to refer a dispute to a body which is unlikely to have a suitable composition for dealing with such cases. This is the Industrial Disputes Tribunal, whose chairman is appointed by the Minister of Labour, and whose two other members are chosen by the same Minister from panels of persons representing employers and workers respectively after consultation with the British Employers Confederation and the Trades Union Congress. It is therefore a matter of great importance to the profession that a properly constituted and independent body to arbitrate on disputes should be speedily set up, that either party to the dispute may resort to it, and that the judgment shall be enforceable, as are judgments against the Crown given in the ordinary courts of law. The arguments for compulsory arbitration are strong, since one side of the Whitley machinery can delay indefinitely. But so long as Whitley machinery is intended for conciliation "it is difficult to believe," in the words of the *Economist*,[4] "that the Whitley machinery can ever work satisfactorily if, as is now proposed, either party to the dispute can take a dispute to arbitration without the consent of the other." These are problems that the profession will no doubt consider carefully.

The Council's proposals will be before a special meeting of the Representative Body on December 13.

[1] *British Medical Journal*, *Supplement*, October 13, p. 141.
[2] *British Medical Journal*, October 13, p. 899.
[3] *British Medical Journal*, *Supplement*, October 30, p. 170.
[4] *Economist*, October 20, p. 908.

One of them recommends that a special court of arbitration should be set up for the Health Service, though it should be noted that no agreement on arbitration can be satisfactory while the Minister retains the powers that he now has under Section 66 of the Act. The court should have a legally qualified independent president appointed by the Lord Chancellor, the appointment—and this should be emphasized—being on a permanent basis. The other members should have special knowledge of the subject matter, and they should be selected in equal numbers by the Lord Chancellor from panels nominated respectively by the appropriate committees of the Whitley management and staff sides. In other words, the endeavour is to obtain a court that will, so far as possible, be balanced in its constitution and independent of whatever Government is in power. The disputants could go to such a court in the expectation of a fair hearing, and the Government could enforce the court's decisions in the knowledge that these had been arrived at by an independent tribunal. If Governments are always to insist on having the last word, to insist on holding a power of veto, doctors will come to regard the State only as a dangerous partisan and themselves as the betting-chips of party politicians.

ASPIRATION PNEUMONIA

One result of the treatment of lobar pneumonia with the sulphonamides and penicillin has been an increasing interest in a group of pulmonary infections which had not previously been clearly separated from the bacterial pneumonias. These pulmonary infections usually give rise to a pneumonic illness which is less severe than lobar pneumonia and in which the physical signs and radiological changes in the chest are less obvious. In the past the understanding of these pneumonias has been confused by the widespread use of such meaningless terms as "pneumonitis" and "primary atypical pneumonia" (which describe neither the pathology nor the aetiology of the complaint) or by the indiscriminate application of the diagnosis of "virus" pneumonia in the absence of any real evidence of a virus infection. Further studies on the cause of pneumonic illnesses of this type have shown that, although some of them may arise from a true virus infection of the lung, the great majority result from a simple mechanical obstruction of a branch of the bronchial tree by infected secretions from the respiratory tract with consequent collapse and inflammation of the corresponding bronchopulmonary segment. To such cases the term "aspiration pneumonia" has been applied—a term emphasizing a common mechanical basis in the aetiology of a protean group of pulmonary disorders which had hitherto appeared unrelated.

In 1939 Ramsay and Scadding[1] drew attention to transient radiological opacities often found in the lungs of patients suffering from mild upper respiratory catarrh. They considered that the opacities were due to segmental or lobular collapse of the lung resulting from the retention or aspiration of infected mucus and consequent obstruction of a segmental bronchus. More recently Scadding[2,3] has emphasized that this type of pneumonia is very common, usually occurring as a complication of acute respiratory infections or sporadically in patients suffering from chronic respiratory catarrh. It is known, of course, that the same mechanism operates in other lung disorders: the pulmonary collapse which sometimes follows surgical operations and which often complicates whooping-cough is due to the obstruction of the bronchi by viscid sputum. Brock[4] has shown that fetid lung abscess is caused by the inhalation of infected material from the teeth or tonsils into the bronchial tree, the site of the ensuing abscess corresponding to the bronchopulmonary segment which happens to be lowest at the time of aspiration. Non-specific suppurative pneumonia, a disease of intermediate severity between acute lung abscess and benign aspiration pneumonia, almost certainly begins in the same way.[5,6] Thus there is good evidence that aspiration of infected material into the bronchial tree can give rise to a whole range of pneumonic conditions varying in severity from benign aspiration pneumonia to acute lung abscess,[7] the factor determining the severity of pulmonary infection being the type and virulence of the bacteria which happen to be present in the retained mucus.

Elsewhere in this issue of the *Journal* Squadron Leader P. W. Robertson and Dr. K. D. F. Morle describe the clinical and radiological features of 500 cases of pulmonary infection which conformed to the usual picture of aspiration pneumonia. All the patients were young men undergoing an initial period of military training. The illness varied in severity from case to case, but was usually mild, consisting of an acute upper respiratory infection which was followed immediately by the symptoms of a pneumonic illness. Examination of the sputum showed only those organisms normally grown from the

1 *Quart. J. Med.*, 1939, **8**, 79.
2 *Lancet*, 1948, **1**, 89.
3 *Proc. roy. Soc. Med.*, 1951, **44**, 511.
4 *The Anatomy of the Bronchial Tree*, 1946, London.
5 Logan, A., and Nicholson, H., *Thorax*, 1949, **4**, 125.
6 Nicholson, H., *Lancet*, 1950, **2**, 605.
7 *British Medical Journal*, 1951, **1**, 685.
8 Quinn, L. H., and Meyer, O. O., *Arch. Otolaryngol.*, 1929, **10**, 152.
9 *Proc. roy. Soc. Med.*, 1951, **44**, 515.

mucosa of the upper respiratory tract, and the white blood cell count was usually normal, although an occasional patient had a moderate leucocytosis. Radiological examination showed that the disease was in all cases strictly confined to the distribution of one or more of the segmental bronchi. In a surprisingly high proportion of patients the basal segments of the lower lobes were affected, a finding which suggests that aspiration took place while the patients were ambulant, since the recumbent posture encourages aspiration into the lower parts of the upper lobes or into the apical segments of the lower lobes.[8]

Robertson and Morle then show that the clinical features of their cases were similar in all respects to those which have frequently been described in outbreaks of the so-called "primary atypical pneumonia." They assert that the misnomer of "atypical pneumonia" has often been used for cases of the type they describe, and they rightly join the ranks of those who plead for the abolition of this cumbersome and meaningless term. But abandoning the use of this diagnosis calls for some caution, since there is a danger that any convenient term which may be substituted will become in time equally meaningless through similar abuse. The statement by Robertson and Morle that "primary atypical pneumonia" represents segmental aspiration pneumonia is not only open to this danger but ignores the possibility that some outbreaks described as "primary atypical pneumonia" were in fact caused by infection with a virus or with *Rickettsia burneti*, the causative organism of Q fever. Marmion[9] found that about a quarter of the cases diagnosed clinically as "primary atypical pneumonia" had serological evidence of infection with a virus, and that in a further 10% there was a significant increase in cold agglutinins or a positive reaction to the *Streptococcus M.G.* agglutinin test. The clinical differentiation between simple aspiration pneumonia and "virus" pneumonia is often difficult or impossible, but on the whole the "virus" pneumonias cause more constitutional disturbance, fail to respond to penicillin, and do not show a strictly segmental opacity on radiography.[3] The difficulty in distinguishing between these two varieties of pneumonia is greatly increased by the probability that virus infections of the upper respiratory tract often give rise to secondary non-specific aspiration pneumonia. The term "primary atypical pneumonia" has served its purpose in emphasizing the frequency of numerous respiratory diseases of differing aetiology, but there is no longer any justification for its continued use. There is little doubt that the majority of cases so labelled will, on closer scrutiny, prove to be examples of the common aspiration pneumonia.

SUDDEN DEATH OF INFANTS

Unexpected deaths of infants in beds, prams, and cots, usually attributed to mechanical suffocation, have been a subject of concern to paediatricians and health officers for some time. This concern has crystallized into preventive measures in the form of publicity for the dangers of soft pillows and the like and legislation against alcoholic mothers. The probable reason for this emphasis on mechanical causation rather than a search for other causes has been well explained by Bain, who suggests that an initial assumption of mechanical suffocation is made because the infant is found with bedclothes on its head or lying on its face. Either there is no supporting necropsy, or a very sketchy one is made in many cases and the textbook signs of asphyxia discovered. The pathologist, with his mind directed to a mechanical causation, seizes on these post-mortem appearances and fails to search for other possible natural causes. This may also be the explanation of a more recent vogue for naming inhalation of milk or stomach contents as the cause of death, and frequently blaming artificial feeding, but disregarding the fact that such inhalations are an agonal manifestation in many anoxial deaths. Werne has rightly pointed out that at the present time in the absence of a distinctive mark of wilful or accidental force it may be difficult to establish positively that death is due to mechanical asphyxia, and such a diagnosis must be at least supported by the exclusion of all other causes.

Dr. D. Swinscow in this issue, by examination of the sex ratios of infant deaths from accidental mechanical suffocation in various circumstances, suggests that the causes of death in cots and cradles differ considerably from the causes of death in bed and by food, and suggests that no death should be attributed to accidental suffocation unless there is clear positive evidence. As such positive evidence is not possible in many cases there seems to be a strong case for refusal to give the cause of death until careful histological and bacteriological study of the body has excluded other causes. Unfortunately such an investigation takes time, and it is impossible for the coroner to await the results without opening an inquest. It is to the public interest that the problem should not be allowed to rest in a state of confusion, and there is a strong case for a full study, including investigation of the home of the dead child by a field worker, such as the health visitor. Such an investigation is already in progress in the U.S.A.

NAEVUS OR NAEVOID?

It seems that in the Latin language the word "naevus" was a lay expression meaning a birthmark, and therefore necessarily lacked scientific precision. It is evident that in its use as a medical term to-day precision is even more difficult to achieve. For a birthmark is something that can be seen and involves the skin, but we know that many of them may be accompanied by specific lesions in the internal organs. When such lesions are present, as they may be, without involvement of the skin, the layman would no longer apply the term birthmark, but

the physician is inclined to keep the same name since the underlying pathology is the same. Through lack of a natural dividing line the group of naevi has, therefore, been most widely extended, as Dr. Parkes Weber points out elsewhere in this issue (p. 992), to include an enormous variety of lesions which have in common only their congenital nature or their proved or presumed developmental origin. Indeed, there are some who would go even further and describe as naevoid such functional abnormalities as the inborn errors of metabolism, the physical basis of which is not yet known. It would be convenient, as Mr. D. N. Matthews[1] has indicated, if the term "naevus" were restricted to "moles"—the benign agglomerations of naevus cells in the skin, though in the case of those moles which first appear in late childhood or adult life it must be remembered that their congenital or developmental origin remains an assumption. For these naevi the common English name of "mole" is as precise a term as any, for alternatives such as "pigmentary naevus," "benign melanoma" and "Schwannoma" are less exact or imply pathological characteristics which are as yet unproved. But, as Matthews admits, it is impossible not to allow the term "naevus" to include birthmarks produced by abnormalities of the blood vessels, and after this admission further limitation in the use of the word becomes arbitrary. Thus it is doubtful if the term retains useful significance.

In common practice we think of the naevi as localized blemishes of the skin which are present at birth or, if they arise later, exactly resemble those that are congenital. Those most often met with are moles and certain vascular abnormalities. The importance of moles is mainly cosmetic, but their rare tendency to malignant degeneration demands attention, particularly when they are, by their site, subject to repeated trauma or irritation. It is generally accepted that, if moles are to be treated at all, they should be removed by surgical excision. No other treatment achieves the same reliability combined with cosmetic result.

The treatment of the vascular birthmarks allows considerable scope for personal preference. The strawberry mark, which is present at birth or appears soon afterwards, is made up of a mass of endothelial cells and perhaps should really be regarded as a benign haemangio-endothelioma. Lister[2] has indicated that the natural history of this lesion ends with its spontaneous disappearance in childhood, but its rapid growth and tendency to ulceration usually make treatment necessary. *X* rays or radium are effective, but the possibility of interference with the growth of subjacent tissues, particularly epiphyses, spells the need for caution. A simple application of carbon dioxide snow is often sufficient, but in larger lesions the injection of sclerosants may be necessary, perhaps combined with surgical operation. Generally speaking these lesions should be treated as soon as they appear.

The port-wine stain, or naevus flammeus, is present at birth, does not grow except in proportion with the rest of the body, and is quite resistant to most forms of treatment. Short of surgical removal, which may present great difficulties to the plastic surgeon, the repeated application of thorium-X offers a prospect of improvement which is sometimes sufficient, and the best prospect of recovery if it is undertaken early in life. This lesion should not be confused with the pale mottled erythema which is so commonly observed over the occiput and over the eyelids of the newborn. This requires no treatment. The erythema of the eyelids nearly always disappears within the first year or so of life; it persists on the back of the neck in about 50% of adults, but is often hidden by the hair.

There is little justification for regarding the spider naevus as a naevus, since its development or congenital origin is evident only in the Osler–Rendu syndrome. In other cases it appears to be more dependent upon oestrogen activity. The diffuse naevi and naevoid conditions seldom offer the same prospect of eradication by treatment, though their effects can often be countered by medical or surgical management. Their study offers a fruitful field to the geneticist.

[1] *Proc. roy. Soc. Med.*, 1951, **44**, 609.
[2] *Lancet*, 1938, **2**, 1429.

NOBEL PRIZE 1951

The announcement that Dr. Max Theiler has been awarded the 1951 Nobel Prize for Medicine for his outstanding work on yellow fever comes within a month of the centenary of the birth of Dr. Walter Reed, who discovered in 1900 that the yellow-fever virus was transmitted by mosquitoes. Nearly forty years later Dr. Theiler, working with the late Dr. W. D. M. Lloyd, a Canadian, in the laboratories of the International Health Division of the Rockefeller Foundation in New York, showed that after prolonged growth in chick embryo tissue and tyrode solution the yellow-fever virus became so attenuated that it could be injected subcutaneously without causing a severe reaction. This strain, the 17 D virus, is now the one used for immunization against yellow fever. It has already been given to more than 40 million people.

Dr. Theiler, who is 51 years of age, was born in South Africa, and is still a citizen of the Union. His father was the late Sir Arnold Theiler, who was for so long the director of the South African Institute of Veterinary Research at Onderstepoort. Max Theiler studied medicine at Pretoria, in Switzerland, and at St. Thomas's Hospital, London, taking the Conjoint qualification in 1922. Shortly afterwards he went to Harvard to work in Dr. Sellard's laboratory. In 1930 he discovered that yellow fever could be transmitted to mice by intracerebral inoculation and that on continued intracerebral passage the virus lost its pathogenicity for the liver, becoming a fixed neurotropic strain. This neurotropic strain, together with yellow-fever immune serum, formed the first effective vaccine. Before it was discovered Dr. Theiler himself contracted yellow fever in the laboratory, but luckily his attack was a comparatively mild one. In addition to his work on yellow fever, Dr. Theiler was the first to discover the encephalomyelitis group of viruses in mice, which resemble poliomyelitis virus and serve as a working model of the human infection in the rodent.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

MALARIA: ITS RECOGNITION, TREATMENT, AND PREVENTION

BY

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There are four recognized species of human malaria parasite—namely, *Plasmodium vivax*, the parasite of benign tertian malaria; *P. falciparum*, the parasite of malignant tertian malaria; *P. ovale*, which gives rise to a particularly mild type of tertian malaria; and *P. malariae*, the parasite of quartan malaria. *P. vivax* has the most extensive distribution, being the predominant infection in most malarious areas within the temperate zone, and also widespread throughout the Tropics and subtropics. *P. falciparum* is common in most tropical and subtropical countries, and is associated especially with hyperendemic malaria, and with the great regional epidemics which occur from time to time in North-west India, Ceylon, and elsewhere. *P. malariae* occurs in most malarious regions, but is less common than either *P. vivax* or *P. falciparum*, whilst *P. ovale* has the most restricted distribution of all. The only fully authenticated records about the last-named species are those of infections acquired in East, Central, or West Africa. Cases have been reported from time to time from other places, but these are generally considered to be of doubtful validity.

Benign Tertian (vivax) Malaria

An overt attack of vivax malaria is in most cases preceded by prodromal manifestations such as headache, lassitude, anorexia, and possibly some gastro-intestinal upset. In the initial stage of a primary attack the fever is remittent in type, rarely exceeding 103° F. (39.4° C.) and is not accompanied by rigors. At this stage parasites are extremely scanty in the peripheral circulation. In the fully developed stage the fever becomes intermittent and the peaks of temperature become higher (often exceeding 105° F.—40.6° C.), each paroxysm being accompanied by a rigor which may last for one hour or more. Numerous asexual parasites in all stages of development from young rings to mature schizonts are now present in the peripheral blood. There follows a hot stage of about four hours' duration, during which the skin is flushed and headache and vomiting are severe; this is succeeded by a sweating stage, when the temperature falls to normal and all the symptoms are relieved. In a primary attack the fever in the developed stage is almost always quotidian.

In a relapse the temperature curve differs from that recorded in a primary attack in that the fever usually shows definite tertian periodicity. Another striking difference is that asexual parasites, all generally in the same stage of development, are present in the peripheral circulation in large numbers on the first day of fever.

Ovale Malaria

Ovale malaria differs from that caused by *P. vivax* in that the disease is in most respects considerably milder. There is an initial remittent stage in less than 50% of cases, rigors are less frequent than in vivax infections, and spontaneous recovery in the absence of specific treatment is comparatively common. It has been observed that febrile paroxysms often begin late in the evening, whereas in vivax malaria they more often occur at about midday.

Malignant Tertian (falciparum) Malaria

Falciparum malaria differs clinically from other forms of the disease in several respects. One of the most striking is the infrequency of rigors at any stage. The primary attack begins with a sensation of chilliness, which is followed by a prolonged hot stage and a moderate amount of sweating. Severe aching pains in the back, legs, and joints are usually a prominent feature, and nausea and vomiting, diarrhoea, and abdominal pain and tenderness are often present. The fever is irregularly remittent, with numerous peaks representing the activity of different groups of parasites. Even in the most severe cases the temperature may not exceed 103 or 104° F. (39.4 or 40° C.), and it may not even reach as high as this. Prostration is greater than in other forms of the disease; the headache is more severe; and vomiting, mental confusion, and torpor are more common.

There is no known disease which may simulate so many other ailments as falciparum malaria, among them being heat-stroke, cerebral haemorrhage, thrombosis or embolism, uraemia, pneumonia, dysentery, and acute abdominal conditions such as acute pancreatitis, appendicitis, and gall-stone or renal colic. The graver forms of falciparum malaria are commonly grouped under such headings as cerebral, algid, dysenteric, or bilious remittent. The onset of the cerebral form may be gradual, beginning with headache, or sudden, simulating heat-stroke or apoplexy. Algid malaria is characterized by sudden collapse, often associated with the vomiting of blood, cramps, suppression of urine, and the passage of blood and mucus in the stools. Bilious remittent malaria is accompanied by nausea, vomiting, jaundice, liver tenderness, and persistent hiccup.

Quartan (malariae) Malaria

The clinical course of quartan malaria resembles that seen in vivax infections, except that an initial remittent stage is less frequent and rigors are less often observed. The temperature curve usually shows evidence of more than one group of parasites, and the fever may be quartan, double quartan, or triple quartan—that is, quotidian—in character. In the primary attack parasites are less numerous in the peripheral circulation than in vivax and falciparum infections, and in relapses they may be so few that they are unlikely to be discovered other than by the thick film method, and then only after prolonged search.

Diagnosis

The only certain means of diagnosing malaria is the demonstration of the causative plasmodium by microscopical examination. In malarious areas the examination of a blood smear for malaria parasites should be a routine procedure in medical practice, whatever may be the symptoms or primary diagnosis. Though the clinical picture may not suggest malaria, it should always be borne in mind that in such regions it is often a complicating factor of other diseases, just as some other infection may complicate malaria. These considerations apply with equal force to patients who have returned from residence in, or from visiting, malarious countries, even though there may be no history of a previous malarial attack.

For the preparation of blood films it is essential that the slides used be scrupulously clean, free from any trace of grease, and without scratches, and that the film whilst drying be protected from dust and flies. The patient's finger should be cleaned with alcohol and allowed to dry completely before being pricked with a cutting needle. The latter may be conveniently mounted in a rubber cork and kept in a small glass tube containing alcohol, but must be allowed to dry before use.

To make a thick film, squeeze the finger until a large globule of blood exudes. Touch this with the surface of a perfectly dry slide and with a circular movement in the plane of the surface make a film about the size of a shilling. Spread the blood evenly with the corner of another slide or with the needle, and keep the film horizontal while drying. The film should be of such thickness that newsprint can just be seen through it when wet.

To make a thin film, the globule of blood should not be larger than the head of a large pin. Apply the end of a spreader (which may be either another glass slide with a perfectly smooth edge or a rectangular cover-slip) to the first slide in front of the drop of blood at an angle of 45 degrees, bring it back till it touches the drop, and allow the blood to spread evenly along the edge. Push the spreader forward along the slide, keeping it at the same angle, and dry the film quickly by waving the slide vigorously in the air. A properly made film should consist of an unbroken sheet one cell thick, the cells almost touching one another but not overlapping.

Films may be stained with either Leishman or Giemsa stain, the latter being generally preferred for use in tropical climates. A rapid method of staining thick films with buffered isotonic Romanowsky stain, introduced by Field, is now widely used. A modification of this method, the J.S.B. (Jaswant Singh and Bhattacharji) stain, has the advantage that it can be used for both thick and thin films. One of the most useful descriptions of these methods and of the techniques employed in the preparation of blood films and in the diagnosis of malaria parasites is that given by Field in 1948.*

There is usually a marked leucopenia within a few hours of the first rise of temperature, though there may be moderate leucocytosis during the early stages of a rigor. The number of polymorphonuclear leucocytes generally falls to about 50%, and the mononuclears rise to about 45%. The greatest number of mononuclears are seen between paroxysms, when they may constitute as much as 80% of the total white cells. The rapid onset of anaemia, hypochromic in type, is an important diagnostic sign, and in an acute attack the reduction in the number of red cells may be as much as one million or more per c.mm. of blood within as short a period as 24 hours.

Another suggestive sign is enlargement and tenderness of the spleen, and there may be liver tenderness also. The spleen is unlikely to be palpable in the first few days of the primary attack, but there is often splenic tenderness before the organ can actually be felt.

Should the fever, or any other symptom, recur with regularity at intervals of approximately 48 or 72 hours, the disease is almost certainly malaria. As noted above, this is scarcely ever the case in a primary attack, but it may be an important diagnostic point in the case of a relapse.

It is important to recognize that parasites may be present in such small numbers in the peripheral circulation during the first few days of an attack that they are not detectable in blood smears, even after prolonged search, particularly when these have been taken at the height of the fever, when they are least likely to be found. In the event of a negative finding, further smears should be examined twice daily for at least a week before ruling out the possibility of malarial infection.

Mode of Action of Antimalarial Drugs

The demonstration of a pre-erythrocytic phase of *Plasmodium cynomolgi* in the liver of the monkey, and of a similar phase of *P. vivax* and *P. falciparum* in man, has shed new light on the chemotherapy of malaria. In theory, a drug may act on the malaria parasite in five possible ways: (1) against the sporozoites when first they enter the human body; (2) against the primary tissue or pre-erythrocytic phase; (3) against the asexual parasites in their erythrocytic phase; (4) against the sexual parasites in their erythrocytic phase; and (5) against the late exo-erythrocytic or secondary tissue phase, to which the phenomena of latency and late relapse in vivax malaria have been attributed. There is convincing evidence against the existence of the last-named phase in falciparum malaria.

The classes of antimalarial drugs in common use are (*a*) the cinchona alkaloids (quinine, "totaquina"); (*b*) the 9-aminoacridines (mepacrine); (*c*) the 4-aminoquinolines (chloroquine, camoquin); (*d*) the 8-aminoquinolines (pamaquin, primaquine); and (*e*) the biguanides (proguanil). Certain of the 2:4-diaminopyrimidines have also given promising results in experimental trials, but these are not yet available for general use.

No drug as yet tested has any demonstrable effect on the sporozoite stage of the malaria parasite. The cinchona alkaloids, the 9-aminoacridines, the 4-aminoquinolines, and the biguanides have a destructive action on the asexual forms of all four species of human malaria parasite in the erythrocytic phase. This was formerly designated "schizonticidal action," a term rendered obsolete by the discovery of pre-erythrocytic schizonts in the liver. The 8-aminoquinolines do not affect the asexual parasites in the erythrocytic phase, but have a powerful destructive action on the gametocytes. They also act on the late exo-erythrocytic forms of *P. vivax*. They have been shown to have an inhibitory effect on the pre-erythrocytic phase of both *P. falciparum* and *P. vivax*, but only when employed in dosage too high for routine use. The biguanides are

*Field, J. W. Studies from the Institute of Medical Research, Federation of Malaya, No. 23. 1948.

the only class of drugs which can be used with safety against this phase, and, so far as is known, they are effective only in falciparum infections. They have no demonstrable effect on the sexual forms of *P. falciparum* in the peripheral blood, but render them incapable of completing their development in the mosquito.

Specific Treatment of Clinical Malaria

It is sometimes stated that specific antimalarial drugs should be withheld until parasites have actually been seen in a blood smear. In principle this is obviously desirable, but in falciparum infections in non-immune subjects death has been known to occur while parasites were so scanty in the peripheral circulation as to be scarcely detectable even after prolonged search. There is, in fact, no safe parasite-density level in malignant tertian malaria. It is my opinion that in a region where falciparum infections are common, when a patient is seriously ill with symptoms which do not clearly indicate some other disease, the administration of a specific antimalarial drug should not necessarily be dependent on the microscopical demonstration of parasites. This applies particularly to patients in coma or with other grave cerebral manifestations, when delay in beginning treatment may prove disastrous.

The chief objects aimed at in the treatment of the clinical attack are the prompt alleviation of symptoms and the radical cure of the infection, with minimum risk of toxic side-effects. Sterilization of the sexual forms of the parasite, so that mosquitoes which may feed upon the patient are unable to transmit the disease to others, is also desirable, and in certain circumstances may be a matter of considerable importance.

Quinine sulphate or hydrochloride, given in a daily dosage of 20–30 gr. (1.3–2 g.), will usually bring about rapid termination of the clinical attack and, in falciparum infections, a high rate of radical cure. This drug is, however, comparatively ineffective against certain European strains of *P. falciparum*. It has no effect on the infectivity of gametocytes to mosquitoes, and in certain circumstances may act as a contributory factor in the precipitation of blackwater fever.

Mepacrine, when given with a loading dose of 600–900 mg. on the first day or first two days of treatment, followed by 300 mg. daily for the following five days, will usually effect a rapid termination of the clinical attack in all forms of malaria, and a high rate of cure in falciparum infections. It does not sterilize gametocytes, and toxic side-effects, though of rare occurrence, are by no means negligible. This applies particularly to the so-called mepacrine psychosis, which may be attended by symptoms of mental aberration or even of maniacal excitement. Another drawback is the yellow discoloration of the skin which sometimes follows the administration of this drug.

Chloroquine brings about rapid alleviation of clinical symptoms in all forms of malaria, and a high rate of cure in falciparum infections. It has the advantages over mepacrine of not tinting the skin and of being less likely to induce disagreeable intestinal or psychotic manifestations. The regimen usually recommended is an initial dose of 600 mg. of the base, followed by 300 mg. six hours later, and a single dose of 300 mg. on each of the next two days. Camoquin, whose action resembles that of chloroquine, has been given in doses up to 400 mg. thrice daily for five days, and is said to be equally effective. Neither of these drugs renders gametocytes non-effective to mosquitoes.

Proguanil, in the absence of reinforcement with some other drug, has a less rapid action on the clinical attack than the cinchona alkaloids, 9-aminoacridines, or 4-aminoquinolines; moreover, it cannot be relied upon to effect radical cure, even in falciparum infections. Both these disadvantages can, however, be overcome by reinforcing a five- to seven-day treatment of 600 mg. of proguanil daily with 600 mg. of mepacrine or chloroquine on the first day. Proguanil effectively sterilizes the gametocytes of *P. falciparum*, a property not possessed by mepacrine, chloroquine, camoquin, or quinine. It is, morever, by far the least toxic of all known antimalarial drugs.

Whatever form of treatment may be adopted for the clinical attack, it is advisable to place the patient on a suppressive regime (see below) for the following eight weeks, to cover the period during which recrudescences are most likely to occur.

From what has been stated above, it will be realized that none of the drugs available fulfils all the requirements postulated for treatment of the clinical attack. Quinine has the disadvantage of its association with the precipitation of blackwater fever, and is comparatively ineffective against certain geographical strains of malaria parasites. The clinical response to mepacrine is rapid in all forms of malaria, but minor toxic manifestations and occasional psychoses of a more serious nature are definite drawbacks. Chloroquine and camoquin are probably the most effective agents for terminating the clinical attack, but a number of toxic manifestations have been recorded with each of them. None of these drugs renders gametocytes non-infective to mosquitoes. Proguanil has an extremely low degree of toxicity and effectively sterilizes gametocytes, but its action on the clinical attack is relatively slow, and it cannot be relied upon to effect radical cure of falciparum infections. Reinforcement with mepacrine or chloroquine, as noted above, overcomes both these defects, and such a combined treatment will in most cases ensure rapid alleviation of symptoms, radical cure of falciparum infections, and sterilization of gametocytes, with minimal risk of toxic side-effects. Neither this regime, however, nor any other of the treatments cited above will prevent the occurrence of late relapses in vivax malaria (see below).

For the dispensary treatment of indigenous populations of malarious countries, most of whom possess some degree of tolerance to malarial infection, a single dose of 300 mg. of proguanil or chloroquine base, or 600–1,000 mg. of camoquin, has proved effective. The extent to which each of these drugs is used will no doubt be very largely determined by their market price.

General Treatment of Malarial Attack

The patient should be confined to bed during an attack, and the bowels kept open by small doses of calomel, followed by salts in the morning if found necessary. During the height of the fever the diet should be restricted to fluids, glucose being given freely, if available. During a rigor, hot-water bottles and several blankets should be provided. Hyperpyrexia may necessitate cold sponging. The headache may be

relieved by aspirin, caffeine, codeine compound, or phenobarbitone. Arsenic in small doses combined with iron is useful in convalescence to combat anaemia.

Emergency Treatment

In the treatment of pernicious forms of falciparum malaria, whether cerebral, algid, or gastro-intestinal, oral administration of drugs is seldom practicable; and since prompt action is necessary to save the patient's life antimalarial drugs must be given parenterally. Mepacrine sulphonate ("atebrin musonate") may be given intramuscularly, 200 mg. being injected into each buttock. Good results have also been reported with intramuscular and intravenous injections of chloroquine. Quinine hydrobromide or dihydrochloride, 10 gr. (0.65 g.) in 20 ml. of normal saline, may be injected *very slowly* intravenously, and repeated in six to eight hours if necessary. The intramuscular injection of quinine, formerly widely practised, is apt to cause necrosis or abscess and is not recommended. There is also some evidence that this procedure predisposes to tetanus infection. As soon as the patient is able to take drugs by the mouth, all further medication should be administered orally. The action of proguanil is not rapid enough to warrant the use of this drug in cases of extreme urgency.

Blood transfusion is indicated in pernicious malaria accompanied by grave anaemia, preceded always by careful cross-matching of the donor's cells with the patient's serum and vice versa. Persistent vomiting may be relieved by injections of 5% glucose in 200–400 ml. of normal saline, repeated if necessary, with the addition of 1 mg. of thiamin hydrochloride for each 25 g. of glucose.

Treatment of Chronic Relapsing Vivax Malaria

The action of the 8-aminoquinolines on the secondary tissue phase of *P. vivax* has already been mentioned. The first of these to be used for the prevention of relapse was pamaquin, which was given in combination with quinine—for example, 0.01 g. of pamaquin concurrently with 10 gr. (0.65 g.) of quinine sulphate twice daily for 10 days. American workers have recently shown that certain other members of this group—for example, pentaquine, isopentaquine, and primaquine—are more effective than pamaquin and less toxic, primaquine being probably the best of the three in both respects. Close medical supervision is necessary, however, with all members of this group of drugs, chiefly because of the occasional unpredictable occurrence of acute intravascular haemolysis. The *routine* administration of these drugs in all cases of vivax malaria is not recommended. They should be reserved for the treatment of stubbornly relapsing cases, more especially in circumstances where there is no risk of reinfection.

Blackwater Fever

This condition is essentially an acute intravascular haemolysis, accompanied by haemoglobinaemia and haemoglobinuria, occurring in individuals who have experienced repeated and severe attacks of falciparum malaria. The onset is usually abrupt, with headache, nausea, vomiting of bile-stained fluid, severe pains in the loins, and marked prostration. There may be a rigor, and the temperature usually rises to 102 to 103° F. (38.9 to 39.4° C.) or higher, and may be either continuous or remittent. The urine is typically dark red to almost black from the outset. At first the pulse is rapid and the blood pressure low, but the latter rises later with the development of renal failure. The patient is now restless and anxious, with marked dyspnoea and collapse. Jaundice is a cardinal symptom, and may appear a few hours after the onset of the attack. Anuria may develop suddenly, presaging uraemia and an early fatal termination. The spleen is enlarged and tender, and there is usually some enlargement and tenderness of the liver also.

The red-cell count may fall by as much as 2,000,000 per c.mm. within a period of 24 hours. The parasitized erythrocytes are among the first to undergo haemolysis, and blood smears taken after the onset of the attack are therefore often negative. Patients who survive the primary manifestations of the disease remain for some days in a precarious condition owing to the intense blood destruction, and, though the urine may regain its normal appearance, heart failure may supervene with a fatal issue. Relapses are common, and severe anaemia of a macrocytic type is usually a prominent feature.

Treatment

Owing to the excessive blood destruction associated with blackwater fever there is always great risk of cardiac failure. Hence the first essentials in treatment are careful nursing and absolute rest. The patient should on no account be subjected to any form of exertion, and should not be allowed even to sit up in bed until the acute stage is past. To counteract the restlessness of mind and body parenteral phenobarbitone sodium has been recommended.

If malaria parasites are seen in the peripheral blood, a full course of treatment with a specific antimalarial drug should be given as described above Neither pamaquin nor any other of the 8-aminoquinolines should be given under any circumstances, and quinine is best avoided. Vascular failure may be treated by intravenous plasma, followed if necessary by intravenous saline solution, which may be alternated with isotonic glucose. The fluid intake should not be less than 2 litres a day, and should be so adjusted that the urinary output does not fall below 1.2 litres.

The administration of alkalis in massive doses was formerly recommended, but it has been shown that a too vigorous alkali treatment may give rise to an alkalosis which itself may impair the excretory function of the kidneys. It is therefore recommended that not more than 20 g. of sodium bicarbonate be given in the 24 hours, and that once the urine has become alkaline only enough be given to maintain a slightly alkaline reaction. If used intravenously bicarbonate solution should never be sterilized by heat.

Should the red-cell count fall as low as 1,500,000 per c.mm., blood transfusion, preceded by very careful blood grouping, is indicated. Good results have been reported following the administration of washed packed red cells resuspended in normal saline solution. The patient should be kept strictly in bed for at least 10 days after the disappearance of haemoglobinuria. Liver extract is useful during convalescence.

Malaria Prophylaxis

As noted above, there is no known drug which acts on the sporozoite stage of the malaria parasite, but there

are two classes of drugs which may prevent the onset of an overt attack: (1) those which act on the pre-erythrocytic phase; and (2) those which act on the asexual erythrocytic phase. The biguanides are the only drugs which can achieve the former effect in non-toxic dosage, and their action in this respect is confined to falciparum malaria. Since, however, they act also on the asexual erythrocytic forms of all species of human plasmodia, their use in prophylaxis is by no means limited to falciparum infections. The dosage of proguanil recommended for prophylactic use is 100 mg. daily for non-immune individuals, and 300 mg. in a single dose once weekly for indigenous inhabitants of malarious areas. A great advantage of this drug is that it can be placed in the hands of laymen for distribution without risk of ill-effect, even should the prescribed dose be grossly exceeded.

The second group of prophylactic drugs, which exert their effect solely by their suppressive action on the asexual erythrocytic parasites, includes the cinchona alkaloids, the 9-aminoacridines, the 4-aminoquinolines, and the 2:4-diaminopyrimidines.

For the effective suppression of falciparum malaria, quinine has to be administered in doses as high as 10 gr. (0.65 g.) daily. Against New Guinea strains of *P. falciparum* even this dosage has proved insufficient. Apart from the unpleasant side-effects caused by the prolonged administration of this amount of quinine, the association of this drug with the precipitation of blackwater fever renders it unsuitable for use as a suppressant in areas where falciparum infections are prevalent.

Mepacrine, in a dosage of 100 mg. daily, is a very effective suppressant of all forms of malaria, provided that the drug is taken for 14 days before exposure to infection and continued for one month after leaving the endemic area, but it has certain disadvantages which militate against its routine use under peacetime conditions. A variable degree of nausea and abdominal discomfort is fairly common during the first fortnight of administration and these symptoms persist to some extent in a small proportion of cases. Headache, insomnia, and giddiness may also occur during this stage, but are less frequent. When taking the drug over long periods a proportion of individuals develop skin lesions, the most common of which is a lichenoid dermatitis affecting chiefly the hands, wrists, feet, and ankles. Yellow discoloration of the skin is also comparatively common.

Chloroquine is probably an even more powerful suppressant than mepacrine, the dosage usually prescribed being 300 mg. of the base (500 mg. of the diphosphate salt) once weekly. Its action resembles that of mepacrine, but it is considerably less toxic and does not tint the skin. The same advantages are claimed for camoquin, in a dosage of 500 mg. weekly.

At present the choice of drug for prophylaxis seems to lie between proguanil and either chloroquine or camoquin. Neither of the last two possesses the very low grade of toxicity which is so remarkable a property of proguanil, rendering this drug particularly suitable for widespread administration among labour forces or other employees recruited from indigenous populations of malarious regions. The comparatively low cost of proguanil and its inhibitory effects on gametocytes are other arguments in its favour. On the other hand, it has been shown that, in falciparum malaria at least, resistance to proguanil may be brought about by irregular or insufficient dosage. It is important therefore to ensure that the drug is taken regularly and in the amount prescribed. It is also advisable in dealing with communities under proguanil prophylaxis to use some other drug, such as chloroquine or mepacrine, for the treatment of overt malarial attacks.

Conclusion

There are many examples of the wide variation in the response of different geographical strains of the same species of malaria parasite to particular drugs. For example, Italian strains of *P. falciparum* have been found relatively resistant to quinine, but readily susceptible to mepacrine. A strain of *P. falciparum* in New Guinea proved resistant to mepacrine, but highly susceptible to proguanil. The existence of strains which are naturally resistant or have acquired resistance to proguanil has also been reported. It is therefore unwise to be too dogmatic on the most suitable form of treatment of malaria in any particular circumstance, and it is fortunate that, owing largely to the enormous volume of intensive chemotherapeutic research carried out during the war, we now have at our disposal a number of specific antimalarial drugs, so that, should a strain of parasite prove resistant to any one, an alternative may be used.

FIVE YEARS OF PROGRESS IN THE HONG KONG HEALTH SERVICES*

BY

I. NEWTON, F.R.C.S.Ed.

Director of Medical and Health Services, Hong Kong

Five years have now passed since the Japanese surrender, and it is possible, on looking back over what has been done, to get far enough away from the trees to see something of the wood.

When news filtered into Hong Kong's prisoner-of-war and internment camps in August, 1945, that the war was at an end, those responsible for the administration of the Colony, including the health services, made their way out of confinement and began a survey of the desolation and destruction left behind by the Japanese.

Nearly two-thirds of the European type of dwelling-houses and about one-fifth of the houses of the working-class Chinese were damaged or in ruins, and, in addition, many public buildings, such as schools, hospitals, dispensaries, and other similar institutions, were destroyed. Those responsible for the administration of the health services set to work without proper office equipment, with a complete absence of all records, and having to rely almost entirely on memories impaired by three and a half years of severe privation. The streets were largely deserted, and the whole Colony could boast of probably little more than 600,000 people, most of whom were suffering from a prolonged period of semi-starvation, and who, like those released from the camps, were unfit for any extended physical effort. There was no public transport, and private cars were a rarity. Antimalaria measures had been neglected for three and a half years,

*Written in 1950.

and malaria had become epidemic; and no real attempt had been made by the Japanese to deal with smallpox and cholera. This was the position in August, 1945. One year later the population was 1,600,000 and to-day is over 2,250,000, which, with the destruction of so much housing, has resulted in serious overcrowding and further complicated the health problems. It is against this background that the present state of the health services and the health of the Colony must be measured.

Temporary Measures on Reoccupation

Within a fortnight of leaving the camps the Colony's health service personnel had opened out-patient clinics and hospital wards, using makeshift equipment left behind by the Japanese. Antimalaria measures of a temporary nature were also started at once, and deaths from malaria, which totalled 765 in 1946, fell successively to 253 in 1947, 193 in 1948, and 116 in 1949. At the present time these temporary measures are being gradually replaced by permanent work, and malaria has ceased to be a threat to the health of the Colony.

Smallpox and cholera, fed by the influx of people during 1946, reached epidemic proportions, and in the winter of 1946–7 there were 1,560 cases of smallpox, with 977 deaths. A vigorous vaccination campaign was instituted, and when the winter of 1947–8 arrived over 2,000,000 vaccinations had been done, and the population was largely immune. Since the spring of 1947, in the three years 1947, 1948, and 1949, a total of only 52 cases have occurred. Cholera was tackled equally vigorously, and many hundreds of thousands of inoculations have been carried out yearly since the reoccupation of the Colony. This, combined with education and regulations concerning the protection and handling of food, has undoubtedly played some part in the disappearance of the disease after the epidemic in 1946.

As more and more of the problems left behind as a war legacy, particularly those connected with personnel, were solved, efforts were made not only to re-establish the health services in existence before the war but to extend and develop them to meet the needs of the vastly inflated post-war population. To follow this development step by step would require many pages of print, and an appreciation of the position reached at the present time is all that can be given.

Progress Made

Perhaps this position can best be understood by examining a few vital statistics. The estimated population of the Colony on March 31, 1950, was 2,357,000. The death rate, based on a figure of 1,857,000, was 8.8 per 1,000 in 1949. The infant mortality rate was 99.4, with a neonatal mortality rate of 29.4. The maternal mortality rate was 2.12, and the birth rate 29.5. Some of these figures have an uncertain factor in the estimated population, but those that depend on registration of births and deaths and on the information supplied in the certificate of cause of death are probably as accurate as in any country where such figures are provided.

The maternity service provides one of the outstanding successes. Out of a total of 54,774 births in 1949, 44,587 were delivered in a hospital or a maternity home, 8,991 were delivered at home by midwives, and only 1,196 (2.2%) of the total births were unattended. Roughly one-third of these cases were dealt with by Government and the remainder by private doctors and midwives. There are 102 small private maternity homes, containing from one to seven beds, run by registered midwives and totalling 333 beds. All these homes and all practising midwives come under the supervision of a senior Government doctor, who combines this supervisory work with the secretaryship of the Midwives Board. In this way a very strict control is maintained over the standards of the midwives.

Another service that has developed considerably since the reoccupation is the tuberculosis service. This is based on the tuberculosis clinic on the island, to which will be added, by the end of this financial year, a second clinic on the mainland. There are 291 Government beds available, of which 58 are reserved for surgical cases; these surgical beds are fed by patients from Government and Government-assisted hospitals. In addition, in the Government-assisted hospitals there are 120 beds in the Hong Kong Anti-Tuberculosis Association's Ruttonjee Sanatorium, and 110 beds for advanced cases in the Tung Wah Group of Hospitals. Survey work is carried out free for all firms or employers of labour who are prepared to undertake responsibility for the medical and social welfare of any patients discovered. An annual survey is made of all Government servants, and legislation is being introduced to provide for a similar survey of all registered school-teachers, private and Government.

The Social Services

There is a limited schools medical service, which provides inspection for all schools, Government and private, and for the medical, dental, and ophthalmic care of children in Government and Government-assisted schools. As these children number only some 17,000 out of a total of about 140,000 schoolchildren, negotiations are in progress with the managers of private schools for an extension of this service to their schools, including in-patient treatment of the children, if necessary, at a cost of $15 a year—that is, rather less than £1 sterling.

There is a social hygiene department running five clinics and a small hospital, one clinic being primarily designed for the use of seamen. This department is staffed by six doctors, one technical assistant, and 25 nurses and dressers.

There are three main infant welfare clinics and three subsidiary teaching centres where attention is not only given to the children and nursing mothers but great emphasis is laid on education. Numerous lectures and demonstrations are given, films and lantern slides are shown, and in 1949 each of the three main centres held a "Healthy Baby Week," which attracted large numbers of visitors, including classes of senior girls from the schools. This has resulted in requests from a number of schools for regular instruction in infant welfare.

Considerable, and increasing, attention is being paid to health education. This is provided by means of a travelling cinema van and public address systems, lectures, posters, and the production of a number of local films. These films have been made by the Medical Department, and have proved a great success. It is hoped to develop this work considerably in the future with the assistance of equipment from the World Health Organization.

Of a different nature but of considerable importance to the Colony is the Port Health work. Here there is a senior Port Health Officer and eight other doctors to

help him. Their activities cover the sea-port, air-port, and the railway terminus. A few figures will perhaps give a better indication of the magnitude of their work. In 1949, 13,707 ships and junks, with over a million passengers and crew, were examined in the quarantine anchorage, 42,000 immigrants were investigated, and 179 ships were fumigated. Nearly 700,000 passengers arriving by train were examined and just over 400,000 of these were vaccinated. Over 4,000 aircraft with 70,000 passengers and nearly 20,000 crew coming from infected ports were inspected. As Hong Kong lies in the midst of endemic areas of plague, smallpox, and cholera, the work of the Port Health Office is of supreme importance.

The Hospitals

Finally there is the clinical side. During the Japanese occupation 400 potential beds were destroyed, and at the present time there are approximately one million more people in the Colony than before the war. Owing to the amount of destruction of buildings in general and to urgent defence requirements, the replacement of these beds has not yet been possible. The demands on hospital facilities, out-patients as well as in-patients, have been so great that it has been almost impossible to meet them. At one large polyclinic on the mainland as many prescriptions were filled during the first quarter of 1950 as during the whole of the previous year, which was in itself an all-time high record. One new polyclinic has been opened on the island, additional doctors have been posted to other clinics, and further beds have been put up in the hospitals. In this way the more urgent demands have been met, and it is hoped that the facilities will become more adequate as the great temporary swelling of the population subsides.

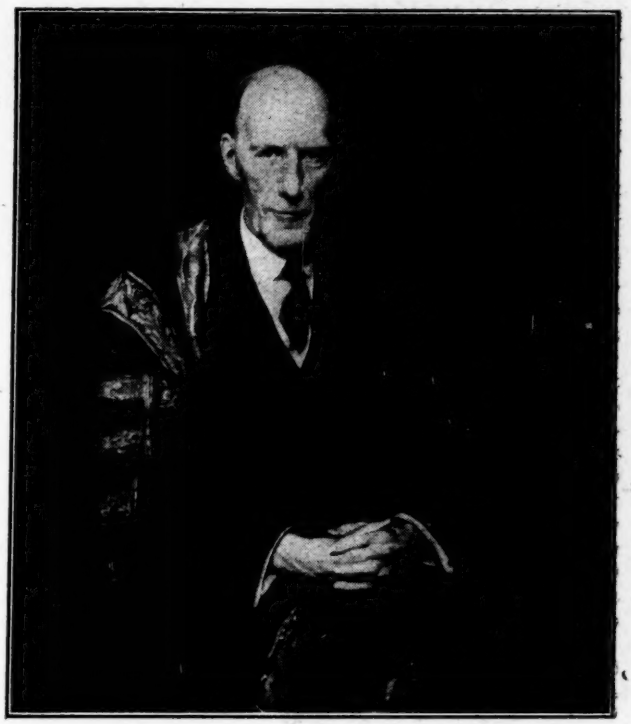
Much has been achieved in five years—but a great deal still remains to be done. Some of this undoubtedly would have been done had there been any interval between the "washing up" after the last war and the "laying of the table" for the next.

[Note.—Since writing the above the second tuberculosis clinic has been completed and is in use, and the schools medical service has been extended to include another 27,000 children.]

SIR ROBERT HUTCHISON, Bt., 80

Sir Robert Hutchison will celebrate his eightieth birthday to-morrow (October 28). In recent years his tall spare figure has been rarely seen in London. He gave up the Presidency of the Royal College of Physicians in 1941 after three years of office, which he said was long enough, and settled in his delightful country house in Berkshire. But although he has forsaken the Whitechapel Road and Devonshire Place and Pall Mall East, Robert Hutchison remains a living force in British medicine, as is clear from the current issue of *Archives of Disease in Childhood*. His sayings, often caustic but always wise, are treasured and quoted, and his students, undergraduate or postgraduate, and those who served with or under him in hospital acknowledge the abiding influence of his personality.

It is 55 years since Robert Hutchison came to London from Edinburgh with the proverbial half-crown in his pocket and a few introductions. He was appointed house-physician at Great Ormond Street, and six months later assistant to Dr. (now Sir) Leonard Hill, then lecturer on physiology at the London Hospital Medical College. Hutchison's classic work, *Food and the Principles of Dietetics*, was first published in 1900, the substance of it having already been given in lectures at the London Hospital and in university extension lectures in the East End. It reached its twenty-fifth printing in 1940, and its tenth edition in 1948. His *Lectures on Diseases of Children* was first published in book form in 1904, and has run through many editions. *An Index of Treatment* first appeared in 1907, and reached its thirteenth edition in 1948. Many writers have contributed to it, but Hutchison has written more than them all, and on a wide variety of subjects. A hand-list of Hutchison's writings has been prepared, including 14 books (without counting separate editions) and over 260 other writings. The list ranges from his *Clinical Methods*, first published in 1897, of which he was the main author, and which has been a working manual for medical students through its 45 impressions, down to the "Retrospect of Medicine" which he contributed to the "Fifty Years of Medicine" number of this *Journal* at the beginning of last year.



But it is not only as a great clinician, a medical teacher, and a "best seller" among medical authors that we salute him. It is as a man of wit and excellence, one who has illuminated medicine by a certain genius which we can only inadequately describe as judgment—judgment which, he said once, was an inborn faculty, a union of mind and character, which a man either had or had not. He has combined an adherence to convention with an open outlook. One piece of advice he gave to students was expressed in a couplet:

> "Be not the first by whom the new is tried,
> Nor yet the last to lay the old aside."

The tradition of Hutchison will live long. His comments and epigrams which made his clinical rounds so lively for his students, and which came out in his lectures and in his general conversation, are still retailed, but above all he will be remembered for his kindness and humanity. Students and many in higher places than students might quail before his rebukes, especially, as one of them has said, when a cold north-east wind was blowing down the Whitechapel Road, but the little girl patients who presented him with a buttonhole during his ward round at Great Ormond Street understood the real man.

His portrait, by James Gunn, which we reproduce, was painted in 1939 and presented to him by the Edinburgh University Club in London. It depicts him in the gold-embroidered black robe of the President of the Royal College of Physicians.

Correspondence

College of General Practice

Sir,—I read with interest the letter from Dr. F. M. Rose and Dr. J. H. Hunt (October 13, p. 908) suggesting the founding of a College of General Practice. No doubt somebody must have thought of this before, but I have never heard of it. Perhaps it was no more than an imaginative idea with no appeal. I think the time has come when such an idea will appeal to many, and it should be given the benefit of serious consideration.

The status of general practice and its future are rightly a cause of concern at the moment. Its prestige has slipped, and quietly at that, because its decline has been brought about by stealth and not by direct intentional attack. Many bodies are concerned with its interests; as we know, two separate committees are now investigating its problems. One of these committees—the General Practice Review Committee of the B.M.A.—may perhaps recommend in its report that a College of General Practice should be set up. It is possible that had there been such a college in the past it would not have been necessary for these two committees to be so busy now.

As science searches into higher fields, specialism inevitably follows, soaring into ultra-specialism. The workaday general practitioner remaining on the ground tends to sink in his own estimation and—maybe subconsciously—in the eyes of the public. The days when all doctors were "doctors" have gone. We are now in one branch or the other of medicine. Is this not an indication that the general-practitioner branch would benefit from having its own parent college?

It may be asked, What could this college do? I think it could do a great deal. Its mere presence would enhance prestige, and it could be a centre round which general practitioners could rally their standards and ideals. The rehabilitation of general practice essentially is not a matter for recommendations or regulations—although the removal of some would help—but is a matter for the whole body of general practice to put right within itself. The college could give a lead.

What practical steps could the college take to achieve its objects? It should not, in my opinion, enter the examination field. Nor should it seek to negotiate where experienced negotiators are already at work. It need not be antagonistic to any existing organization; it could certainly be complementary and co-operative. It could also co-ordinate. Out of the investigations of the two committees now investigating general practice will come recommendations some of which will be sure to be concerned with long-term policies. The implementation of these policies should form a very useful basis for the new college to work on. After all, general practice has not only to be rehabilitated but it also has to be maintained in good health. Is it not in this respect that one central body concerned with one object only would be so valuable?

Broadly, I would say that a College of General Practice should have as its guiding charter the task of seeing to it that general practice becomes, and continues to be, a branch of medicine which will be entered eagerly, practised with satisfaction, and retired from with regret.—I am, etc.,

Brighton. John Thwaites.

Sir,—Dr. F. M. Rose and Dr. J. H. Hunt (October 13, p. 908) surely deserve warm thanks, especially from their brother practitioners but scarcely less from the medical profession and the community it serves, for their suggestion of a College of General Practice. Some think worse than others of the present state of general practice and the prospects before it, but very few can feel happy or confident about it. It is at least a common opinion that our freedom is curtailed, the range of our professional activity contracted, and our standing, whether in the profession or the community, lower than it has been or ought to be. It is notorious that the abler students neither choose nor are encouraged to choose general practice as a career.

To visit the Valley of Humiliation is doubtless good for us all, but to live there is not good for men who, if they are to give good service, must be proud of themselves and of the work they do. In that valley, it seems to me, we are. We hear dwellers on the Delectable Mountains praising us as "spear-heads," "back-bones," or "lynch-pins," but it does not help much. We must find our own way out or stay where we are. I own I find it a little hard to bring the proposed college down to earth, and I doubt if I want it modelled too closely on the existing Royal Colleges, but that some such body is needed I feel quite sure. It would stand, I take it, less for general practitioners than for general practice, aiming to mainstay its standards, restore and enlarge its prestige, and speak for it, when necessary, within the profession and without. Perhaps its most important function would be to restore our pride. I hope this brave conception will be pursued.—I am, etc.,

London, N.W.3. Lindsey W. Batten.

Sir,—Any effort to advance the prestige of general practice and facilitate its working is of the highest value to the whole profession and to our patients. I have hastened to direct the attention of the authors of your admirable letter (October 13, p. 908) to earlier writings urging attention in medical reform to "General Practice: the Gateway to National Health" (*British Medical Journal, Supplement*, 1942, 2, 21).

One specific to restore the dignity of practice now that there is a general resumption of building is the inclusion of the general-practice hospital annexe. This does not mean the questionable health centre, but the urban equivalent to the rural cottage hospital. It is an incalculable boon in a population almost stripped of domestic aid when illness of less major kind supervenes; and to the doctor a minor temple of Aesculapius where he can exercise his trained faculties with satisfaction and sense of achievement, which otherwise are suffering atrophy in the commercialized conditions of practice now prevailing. Incidentally, even the preservation of the priceless asset of the country hospital itself now needs fighting for.

As with the attainment of fine growth in many a plant, so the renowned family doctor—"the flower of our civilization"—depends on right conditions for his cultivation. Society needs reminding that the soil of practice can become impoverished. The patient likes to speak of "my doctor" and so does the latter of "my patient." But is there not a danger that they are ceasing to feel it?—I am, etc.,

Bristol. A. Wilfrid Adams.

Sir,—I have felt for a long time that the education and postgraduate work of general practitioners cannot adequately be dealt with by bodies mainly composed of specialists and consultants.

None but thoughtful general practitioners know the shortcomings (and their remedies) of general practice in standard, status, and relationship to consultants, and a College of General Practice as discussed by Drs. F. M. Rose and J. H. Hunt (October 13, p. 908) would be the ideal tool to elevate general medical practice to its rightful place in the realm of the science and art of healing. May I suggest that such a College of General Practice should not be a negotiating but an academic, educational, and status-raising body? As we general practitioners see medicine in our daily work in its broadest aspects and in its relationship to all human activities, so would such a College of General Practice, in contrast with the specialized outlook of the older Colleges, unify medicine again, and also be able to study and present the part we play in our society and civilization.—I am, etc.,

Southall, Middlesex. M. B. Clyne.

SIR,—The letter from Drs. F. M. Rose and J. H. Hunt (October 13, p. 908) is opportune. The idea of a Royal College of General Practice is of course by no means a new one, but there are a number of special factors in the present situation which suggest that it might well be reviewed afresh. In addition to the important advantages which the writers indicate, such a college would tend to balance the political scales, at present somewhat overweighted on the consultant side, and would command the attention of a section of the public who view with reserve the pronouncements of the General Medical Services Committee. It would, moreover, help to hold the balance between private practice and State practice, and so to resist the dangerous trend towards a State monopoly in medicine.

Should such a college be formed, it would be of the first importance to ensure from the start that it had a proper democratic constitution so that the governing body would be elected by the ballot of the entire membership.—I am, etc.,

Orpington. A. C. E. BREACH.

SIR,—For far too long has the general practitioner meekly accepted the dictum of the hospital specialist that Father Knows Best. Father knows how to train him, teaching him much about Sjögren's disease, nothing about influenza. Father conducts a refresher course, showing off his knowledge of the latest E.C.G. lead, while ignoring Mrs. Jones's wind round the 'eart. Father thinks the general practitioner cannot diagnose early cancer, and is sure it would be disastrous for him to have direct access to an *x*-ray machine. Father is so darned superior, and the general practitioner is a dogsbody.

It is refreshing beyond measure to read the letter of the rebels, Drs. F. M. Rose and J. H. Hunt (October 13, p. 908), who advocate a College of General Practice. The suggestion is not new. Mr. T. B. Layton once proposed it in the *Lancet*. I even suggested it myself (*Modern Trends in Public Health*, 1949, p. 132). But no one hitherto took it as anything but a bad joke. It was ahead of public opinion then, but the denigration of the general practitioner over the last few years may at last make it a practical proposition.

There is no doubt that a college would be of inestimable value. The N.H.S. does not seem to have improved our ethics or standards of courtesy to one another. The influence of general practitioners on both undergraduate and postgraduate training is negligible. The general practitioner receives no encouragement to become a good general practitioner and no recognition if he is. Merit awards are exclusively for Father.

The general practitioner is the only person who is able to see the patient and his environment as a whole; he is our only defence against those who, knowing more and more about less and less, subdivide patients with more than the Chinese thousand cuts. It is high time he asserted himself, for his own good and for the good of medicine.—I am, etc.,

Ashtead, Surrey. W. EDWARDS.

Tuberculosis in School

SIR,—The report on the tuberculosis epidemic (October 6, p. 828) has more than a local interest for us in Glamorgan. It is, however, regrettable that the part played by the general-practitioner service in the discovery of this outbreak was not properly and fully acknowledged. Indeed, had it not been for the vigilance of the general practitioners for the locality in question it is reasonable to suppose that this epidemic would never have come to light. It is therefore disconcerting and most certainly discouraging to find that complete credit for the discovery was given to the paediatrician. This is yet another incident symptomatic, we fear, of an insidious present-day process calculated to undermine the status of the general practitioner, who, to the detriment of the Service, has come to be regarded as one whose sole responsibility is to appease the multitudes besieging his surgery.

However elaborate the superstructure, in the form of specialist and hospital services, no comprehensive health scheme will work efficiently without the active co-operation of the general practitioner who is made to feel that he has a useful part to play in the Service as a whole. Nowadays, to our sorrow, he is the one who is belittled and, more often than not, ignored.—We are, etc.,

Glamorgan Local Medical Committee. E. J. REES, Chairman. D. C. HOPKINS, Secretary.

SIR,—Drs. R. T. Bevan, P. T. Bray, and J. F. Hanly have published an article (October 6, p. 828) in which they give details of an outbreak of respiratory tuberculosis in a school. As the general practitioners concerned with the care of these children from the first instance to the moment of writing, we may perhaps be able to make some useful comment. They stress the need for co-ordination between the various elements in the health service. We maintain that the natural co-ordinator is the general practitioner. We intend to give a short account of the part played by the practitioners in this outbreak, as we think it serves to underline the importance of the general practitioner in this respect.

The outbreak presented itself in the following way, the majority of cases occurring in one practice. Late in June a child recovering from severe tonsillitis continued to be pyrexial after all signs of tonsillitis had cleared. Shortly after this she developed erythema nodosum. A provisional diagnosis of primary tuberculosis was made and the child was admitted to hospital for investigation. Concurrently with this a second child living some distance away continued to be pyrexial after severe chicken-pox, from which she had not made the normal rapid recovery. Having the first case in mind, we again made a provisional diagnosis of primary tuberculosis and the child was admitted to hospital for investigation.

Although these two children lived some distance apart we knew that both attended the same school, and it occurred to us that there might be a source of infection in the school. This was suggested to the paediatric department of the hospital, but in view of the fact that the diagnosis had not yet been confirmed we considered it unwise to create alarm by informing the school authority.

A third child continued pyrexial after mild gastritis which followed an outing to London. She also was sent by us for investigation and was confirmed as tuberculous in early July. Two more children became pyrexial, and to one of these the paediatrician was called on a domiciliary visit.

The diagnosis of primary tuberculosis was confirmed in all these cases, and shortly afterwards the public health department began the Mantoux testing of all the children in the school. The necessary *x*-ray pictures were taken at the chest clinic.

So the outbreak began. The provisional diagnoses were made by the practitioners concerned, and the cases were brought to the notice of the paediatrician when they were admitted for investigation. The general practitioners, having considerable local knowledge, were the first to realize the possibility of a source of infection in the school.

The second phase of this outbreak was the routine skin testing of all the schoolchildren in July, and this revealed a certain number of primary infections. We were notified of the results of these investigations.

On the afternoon of July 14 one of us was called to attend a woman who had been taken ill at the bus stop. This was the school-teacher and she had had a haemoptysis. She was subsequently radiographed and found to have pulmonary tuberculosis.

The next mass skin test was not until November. Between July and November we were consulted by a great many anxious mothers with their children. Some of these we discovered had been missed in the school investigation of July, and we accordingly made arrangements for their investigation at the chest clinic. Others who had had a negative Mantoux in July developed symptoms which justified investigation and were also sent by us to the chest clinic. Three of these were discovered to have a primary tuberculosis complex.

By November we had 12 children in bed with primary tuberculosis. Three of these had been in hospital during the period of investigation, but all were now at home. We were concerned lest there should be a spread of the lung lesion either by extension into the lung or to some more distant field such as the meninges. Accordingly we examined these children daily while they were pyrexial. In December one child (the first of the series) became pyrexial again after a quiescent period. We arranged for this child to be readmitted to hospital, and she subsequently developed a small interlobular effusion which was still present when she was last radiographed.

All these children have been radiographed at intervals since their illness began. This involved a journey of some seven miles to the chest clinic. We arranged the day with the chest physician, and at the time appointed an ambulance collected the children. They were accompanied on each occasion by our secretary, who provided biscuits, etc. This event was regarded by the children as a picnic and a welcome change from the monotony of bed-rest.

In general we accepted the recommendations of the chest physician with regard to the amount of bed-rest. But we modified this occasionally as we thought fit. Here we think it is worth comment that while some children stayed in bed as instructed others were not so co-operative, and one boy repeatedly slipped away to play football and ride horses. His recovery has not been delayed in comparison, and there seems to be no relationship between the time spent at rest and the time taken for recovery in those cases that had no constitutional symptoms.

During this time it will be seen that a great deal of the work was done by the general practitioners, who supervised the care of the children in their homes and made any arrangements necessary for treatment and investigation. Sufficient has now been said to demonstrate our main point, that the key to successful co-ordination is the general practitioner. In this instance we think that, if there is anything remarkable about the prompt detection and, to date, fortunate outcome of this outbreak, it is in large measure due to our use of and co-ordination of the paediatric unit, the tuberculosis service, and the public health department.

In conclusion there are two points of interest. The three cases which had the most marked and prolonged pyrexia, and who were, in other ways, clinically worse than the rest, occurred at the outset and were responsible for drawing attention to the outbreak. In all three there was a history of some minor illness (tonsillitis, chicken-pox, gastritis) occurring during the "incubation period" and coming shortly before the development of symptoms due to tuberculosis. We have noticed this relationship on other occasions when primary pulmonary tuberculosis has presented itself closely after one of the infectious diseases of childhood, commonly measles.—We are, etc.,

Llantrisant, Glamorgan.

J. C. R. Morgan.
E. G. Jones.
D. R. Morgan.

Riding for the Disabled

Sir,—Some time ago I requested information about riding for the infirm. I had in mind at that time a patient suffering from disseminated sclerosis. I had a long letter from Dr. W. R. Monteith, of Lincoln, who was a master of fox-hounds (M.F.H.), in which he gave advice about saddlery and the various ways of mounting adopted by aged and infirm riders he had met. He appeared to be very keen on the cowboy saddle for infirm riders.

I have picked the brains of experienced riding-masters like Mr. Harry Monks and Mr. J. B. Gloster. Mr. Harry Monks advises a saddle into which the rider sinks. The saddle consists of an old police saddle stripped of its leather and replaced by felt covered with soft basal leather. I have ridden in one of his saddles and it is very comfortable for anyone.

Mr. J. B. Gloster has invented a pair of bars which fit any saddle (child's or adult's). These bars, fitted to the saddle, clasp over the middle of both thighs. They are really spring-like horns which when they have been elevated past a certain point open forwards releasing the rider completely. While in position they give a mild restraining feeling over the thighs which gives the rider confidence. They have been used by a patient suffering from early myasthenia gravis.

Messrs. Champion and Wilton, of Oxford Street, London, make a special saddle for patients wearing an artificial limb. This saddle has an extra heavy leather flap on which are two ledges or rolls for supporting the leg. They have made a saddle on this principle for a person who has lost both legs.

I consider that this saddle would wear very well, although it might not be as comfortable as the "Monks" saddle.

Orthopaedic Appliances Supply, 226, Goswell Road, London, E.C.1, make a special prosthesis for riders. I understand that this prosthesis was used by some cavalry officers before the last war.

One M.F.H. who had lost his leg had a special pocket made for his stump and he hunted without his prosthesis. I should not advise this method, as it might lead to embarrassing moments if the rider became parted from his mount.

I have experimented with the horse that I am training specially for the invalid rider with a sponge numnah strapped to the ordinary saddle by a roller over the girth, and I find this adds to the comfort of the rider. I think this would be ideal for the rider wearing callipers, the rings of which would slip off the seat of an ordinary saddle, and this gives the necessary resilience.

The subject is very individual in character. Each case would require to be considered by itself, taking into account disability, riding experience, and mount. I see no reason why more disabled people should not ride either again or for the first time.

The patient for whom I made the original inquiry I learned later became too ill to be able to continue with his proposed riding. I have picked the brains of the individuals mentioned, and attempted to pick the brains of many more from both sides of the Atlantic who regretted that they knew nothing about the subject.—I am, etc.,

Brighton.

W. J. Hastings Sayers.

Surgery of the Parotid

Sir,—I am particularly interested in the subject of the dissection of the facial nerve in its parotid course, and would like to make some observations on this matter after reading the timely article on this subject by Mr. H. S. Shucksmith and his colleagues (October 6, p. 830).

They are surely right in exposing the main trunk of the facial nerve early in a parotid dissection and from there to follow it forward as it branches in the superficial portion of the gland. This can well be done, however, by an incision in front of the pinna prolonged into the classical hockey-stick below the angle of the jaw. The posterior border of the superficial part of the parotid gland is defined and retracted forwards, the styloid process can now be palpated high up between mandible and pinna, and the facial nerve trunk can be dissected out as it lies on the neck of the styloid. Thus a total parotidectomy becomes possible by tracing first the trunk and then the branches of the facial nerve forwards. A temporary facial palsy often results, but this clears up in two to three months.

I would like to support Hamilton Bailey's contention that the parotid gland is bilobed. There is certainly a part of the gland deep to the facial nerve trunk. This was beautifully demonstrated in a patient of mine who had an adenoma of the deep part of the gland with the trunk and the two main branches of the facial nerve stretched tightly on its superficial aspect. It is true that as the nerve goes forwards it becomes intimately connected with the superficial part of the gland, but there is little doubt that all the branches can be dissected out intact provided they are tackled from behind and traced forwards.—I am, etc.,

London, N.21.

W. Garden Hendry.

Sir,—Mr. H. S. Shucksmith and others suggest (October 6, p. 830) exposing the facial nerve at its emergence from the stylo-mastoid foramen, but do not state how many cases they have done. There are serious objections to this approach via the tympanic plate:

1. The parotid gland varies considerably in its size, and frequently extends round and behind the tympanic plate and over the mastoid process.
2. The majority of tumours occur near the main stem of the facial nerve, and there is danger in cutting into or putting considerable pressure on the tumour.
3. This approach gives a very limited exposure in a wound which, with a large tumour, can be of considerable depth.

I have done 25 resections of the parotid gland with preservation of the facial nerve, and have not failed to find the

cervical branch in any of them, but in three cases this nerve ran into a malignant tumour, and recourse was then had to the approach used by Mr. Shucksmith. I have assisted other surgeons to do the operation and am sure that it is a much easier approach for the beginner, as it leads him to the facial stem at the correct depth and enables him to dissect superficially to the nerve with confidence, rather than working down on to so important a structure.

When all the branches of the seventh nerve have been preserved, full recovery of facial movements has occurred in my cases. I have not yet had a recurrence after resection for a clinically non-malignant tumour, although several cases had had one or more previous operations elsewhere. However, I am glad that other surgeons are performing this operation, which is, I believe, the operation of election for simple tumours and mixed parotid tumours, but, except in special cases, it is unwise in the presence of clinically malignant tumours.—I am, etc.,

Carshalton, Surrey. HENRY A. KIDD.

Rupture of the Spleen

SIR,—The letters of Mr. N. N. Iovetz-Tereshchenko (September 8, p. 608) and Dr. J. E. S. Stephens (September 22, p. 739) prompt me to record a similar case.

A perfectly healthy boy, aged 10, while running to school in the morning of May 6, 1949, tripped and fell flat on his stomach. His mother brought him to see me soon after the accident. The boy complained of some vague pain in the epigastrium, but appeared otherwise normal. I advised the mother to keep him at home for the day. I was urgently called to see him an hour later. The boy appeared to be very shocked; he had a thready pulse, was very pale, and sweated profusely; he complained of pain at the tip of the left shoulder, and his upper abdomen was tender. I diagnosed an intra-abdominal haemorrhage due to a ruptured viscus, probably spleen. I got him admitted, after some difficulty, into a hospital and mentioned the provisional diagnosis of a ruptured spleen. On admission there the boy was shocked and had a rigid and tender abdomen—right hypochondrium more than the left. He was provisionally diagnosed as a ruptured liver. He was operated on: a right paramedian incision was made and much blood in the peritoneal cavity was cleared away. No ruptured liver was found, but the spleen had been severely damaged and was found to be almost completely divided across. Splenectomy was performed. Intravenous blood was continued and his condition was good after 24 hours. He made an uneventful recovery and was discharged on May 18.

Rupture of the spleen, although uncommon, should always be borne in mind after an abdominal injury. The interesting features of this case are: the latent period of absence of any symptoms; a positive Kehr's sign (referred pain to the tip of the left shoulder) when seen at the onset of the shock; normal healthy spleen (non-malarial) not abnormally fragile; the misleading clinical picture on admission into the hospital two hours after the accident, which led to a provisional diagnosis of a ruptured liver being made.—I am, etc.,

London, S.E.25. A. FRY.

Removing Large Numbers of Teeth

SIR,—We were very interested in Dr. A. Barham Carter's letter in your issue of October 6 (p. 850). While we concur with his remarks on the general undesirability of mass dental extractions, it must be realized that for a variety of reasons, social, psychological, and economic, such extractions are frequently necessary. We deplore the treatment of mass extraction as a minor procedure, and are of the opinion that each case calls for the fullest co-operation of doctor and dentist to minimize trauma and ensure freedom from infection, both by pre-operative dental hygiene, adequate medical examination, and the use of antibiotics where considered necessary.

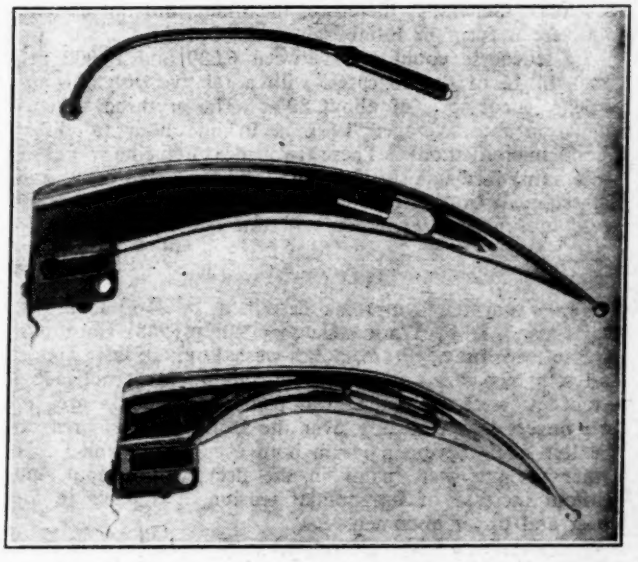
It has been our practice for some time past to perform the extractions in the local hospital out-patient department. This is an ideal arrangement, but any place where a couch is available for recovery will serve. Patients are instructed to report one hour prior to operation, after a light breakfast. Premedication is by 1/100 gr. (0.65 mg.) atropine. Anaesthesia is induced with a small dose of thiopentone (usually less than 0.5 g.) and maintained with nitrous oxide, oxygen, and "trilene," through a naso-pharyngeal tube, with the oral cavity packed off. With this technique it is possible to give a continuous and readily controlled light anaesthetic, and at the same time allow the dental surgeon a completely clear operating field. There is no technical difficulty in passing the naso-pharyngeal tube, and a simple anaesthetic machine is all that is required. The dental surgeon is relieved of all sense of urgency, whether from his colleague or his patient, and thus is able to perform more gentle extractions with far less risk of damage to the alveolar structures. Further, another predisposing factor in the causation of post-operative infection, the massive local anaesthetic, is removed. Recovery is not delayed, and patients are fit to go home within an hour or two.

Using this technique, we have largely avoided the pitfalls outlined in Dr. Barham Carter's letter, and our patients have frequently been pleasantly surprised at the small amount of trouble they have had in surmounting what they expected to be a considerable ordeal.—We are, etc.,

R. PALMER.
Monmouth. J. L. INSLEY.

Modification of Macintosh's Curved Laryngoscope

SIR,—This laryngoscope is designed primarily to facilitate the passing of an oro-tracheal tube in the difficult patient with prominent teeth and receding jaw. The blade is an inch (2.5 cm.) longer than Professor Macintosh's and the curve on it is less. The two blades are shown together for comparison. Professor Macintosh has described (*Lancet*, 1944, **1**, 485) blades of varying shape all passing in front of the epiglottis. The curved blade which he favours is



easier to introduce and an excellent view of the larynx is obtained; but in some cases unless a similarly curved tube is at hand intubation can be extremely difficult.

Using this modified blade, I found the lessened curve on it enables the tube to be passed with much greater ease, while maintaining the advantages of an anterior approach to the epiglottis. The greater length is an added advantage in the larger patient. The separate bulb assembly is another feature of the blade (see photograph) to facilitate cleaning.

I would also like to thank Dr. H. L. Thornton for some helpful suggestions, and also Mr. A. Charles King, who arranged for the instrument to be made by the Longworth Scientific Instrument Co., Ltd., Thames Street, Abingdon, Berks. Acknowledgments are also due to the photographic department of St. Mary's Hospital.

—I am, etc.,

London, W.2. CYNTHIA M. PARROTT.

Bornholm Disease

Sir,—I was interested in the report by Drs. J. B. M. Davies and J. F. Warin of an outbreak of Bornholm disease in Oxford (October 20, p. 948), since a similar epidemic occurred in the Edinburgh area in May, June, and July of this year. The clinical picture corresponded generally with that described but differed in a few particulars, which may be of interest.

Eighteen children suffering from Bornholm disease were admitted to the Royal Hospital for Sick Children, Edinburgh, between May 1 and August 1, and many more cases were seen as out-patients. The striking feature was the occurrence of the pain in two distinct phases in many of the patients. Lower thoracic or upper abdominal pain, of sudden onset, was present intermittently for about one day, followed by a period of one to three days in which the child was apparently well, though anorexic. The pain then recurred for a further day or two before finally disappearing. Twelve of the eighteen children showed this clear-cut periodicity.

The pain was usually spasmodic and very severe, one child being sent in with the diagnosis of angina pectoris, as the doctor had never seen such severe pain in a child. Typically, the children were in pain rather than ill, the reverse picture from pneumonia, where general symptoms usually overshadow the pain. The temperatures recorded were lower than those in the Oxford outbreak, being usually 99° to 100° F. (37.2-37.8° C.), and in no case did the temperature on admission exceed 101° F. (38.3° C.). Signs of meningitis were not seen in any of our cases, but six of the eighteen children had slight faucial injection. All the children had anorexia, but only five vomited at the onset, and none had diarrhoea. All but one of the children were between 2 and 6 years of age and some may have had slight headache without complaining, but in no case was a history of headache elicited, in contrast with the severe symptoms noted in Oxford.

Recovery in all our cases was rapid and complete, and we did not see the debility and tiredness following the attack, which has been apparently so common in the Oxford epidemic. Generally, therefore, the illness did not assume so severe a form in Edinburgh as in Oxford.

The leucocyte count was between 6,000 and 13,000 per c.mm. in 16 of the 18 cases, with a relative polymorphonuclear leucocytosis of about 80%. The erythrocyte sedimentation rate averaged 19 mm. in one hour (modified Cutler micromethod). These two measurements were of some value in diagnosis, since the total leucocyte count and the sedimentation rate are usually considerably higher in acute tonsillitis or pneumonia at this age.—I am, etc.,

Edinburgh. R. G. Mitchell.

Sir,—From the symptoms described by Drs. J. B. M. Davies and J. F. Warin (October 20, p. 948) Bornholm disease was prevalent in South-west London last winter, and was recognized as a virus infection. Most noticeable symptoms were the acute head pains, localized in area to two fingers laid vertically over the fronto-parietal area on the left side. Severe pains in both eyes accompanied this. Other variants were pains in the neck and occiput, but without increase of intracranial tension, and pains in the chest and upper abdomen.

Some of those with pains in the chest were the only cases requesting visits, as anxious parents feared pleurisy. These pains were usually on the left side (eighth to tenth costal areas), or in a continuation of this area to the left upper abdominal wall. Radiographs were invariably negative. All seem to have recovered completely, and few children were affected.

What is more worrying now is what I am now beginning to realize is another virus infection—labyrinthitis.

The first case began 18 months ago. The patient had malaise, deep depression, giddiness, and five attacks of severe vertigo which made her crumple as though hit by a hurricane. The condition cleared completely in two weeks. Therefore I was the less concerned when milder cases presented themselves. But they are not all clearing in two weeks. Some are prolonging into months. Hearing appears to be unaffected; but the patient is afraid to turn her head, or to go out alone. There have been two cases in one family; but so far no child has been affected.

I am hopeful that this may be a condition which can be cured by antibiotics.

In view of the possibility of serious and handicapping after-effects, it seemed justifiable to try the result of giving "chloromycetin" to my last patient, a happy young mother with a family at school. She was feeling "awful," too giddy to move, and her daughter had to remain at home to help. Starting to take chloromycetin 36 hours after the commencement of her illness, she improved rapidly, and three days later felt recovery complete. For this reason the case is worth reporting in the hope that others may repeat the result.—I am, etc.,

London, S.W.4. Marguerite Stewart.

Sir,—The action of the medical officer of health of Oxford in warning medical practitioners of the outbreak of Bornholm disease is very right and proper. Newspaper reports refer to the condition as being a rare disease, but it would be more correct to say that the disease has been largely ignored. My personal experience is that epidemics have occurred regularly in the country for at least the last five years, and inquiry reveals that others working in different parts of the country have had the same experience. Why, despite many articles in the medical press, is the condition not widely recognized? There are several probable explanations which I will not discuss. I do, however, wonder how often laparotomy is performed, or how often prolonged investigations are carried out to determine the cause of a mysterious orchitis.—I am, etc.,

Farnborough. D. P. van Meurs.

An Egg Muddle

Sir,—You rightly say in your leading article on "Our Daily Bread" (October 13, p. 896), "The provision of food in its natural state is obviously desirable," and, one might add, as fresh as possible. In this connexion the following facts, which I verified two days ago, may interest your readers and even the general public.

The Wrenbury Colony in Cheshire exists for the recovery and rehabilitation of tuberculous patients, and one of its most suitable industries is egg and poultry production. It is therefore an accredited poultry-rearing establishment, and as a result its total egg production has to be sent to the local egg-packing station if it is to get its full ration of feeding-stuffs. It is not allowed to retain any of its fresh eggs for the benefit of the tuberculous patients, and the combined efforts of the Ministries of Food, Agriculture, and Health ensure that they get "shop eggs" instead.

Numerous efforts to alter this Gilbertian and most unsatisfactory arrangement have all failed because it is apparently administratively impossible. It is to be hoped that if we get any new Ministers in these departments after the election they will mark their arrival by doing at least one common-sense thing for the benefit of the public rather than for the convenience of their officials or the integrity of their red tape.—I am, etc.,

London, S.W.1. W. N. Leak.

Plain Words

Sir,—His Majesty's Stationery Office has recently published a booklet entitled *A.B.C. of Plain Words*, by Sir Ernest Gowers. This work is an attack on jargon and officialese, and many of your readers may have seen Mr. Ivor Brown's amusing review of it. After quoting the following howler from the book: "The actualization of the motivation of the forces must to a great extent be a matter of personal angularity," Mr. Brown concludes that jargon is a kind of uniform. "The English," he says, "love to wear ritual clothing in civil as in Service life and so cherish a ritual verbiage too."

I hope doctors felt warm under their white collars when they read that. For when one doctor communicates professionally with others, even in the pages of this very journal, what a weight of jargon clogs his words. To begin with, he will not write in the active voice. Never does one read in a paper, "I thought this," "I did that," but instead an eternity

of "It was evident that . . ." "It is emphasized that . . ." "It was felt that . . ." Goodness me, many writers do not stop short of "It was felt that the swelling was enlarging."

Nor do we lag behind the Civil Service in fondness for the abstract. Our penchant is for -age and -ability—the operability of the tumour, the fatigability of the muscle, or the mouldability of the foetal head. We say the dosage of a drug when we mean the dose; but again for the worst examples we must turn to our obstetric colleagues, who have given the world the twin monsters "foetal wastage" and "foetal salvage." They ought to call meconium "foetal sewage." The expression "obstetric colleague" is also anathema. We do not, mercifully, talk of pathologic colleagues, though I have seen in a paper acknowledgment to Dr. Blank for his anaesthetic excellence.

The laity are perhaps responsible for "check-up," but the profession must take the blame for "follow-up," which can be a verb, an adjective as in "follow-up clinic," or a noun as in "at follow-up six weeks later. . . ." Then we have the hard-worked verb "to present," sometimes in our hands curiously intransitive: "The patient presented with the following symptoms." We talk of "the overall clinical picture" for all the world like Charles Suet, and we ask a great deal of "history": "There was nothing relevant in the gastric history." "Superimposed" is another favourite, and we often hear of pneumonia being superimposed on an underlying bronchiectasis, or, perplexingly, on a long-standing one. Or we are told that the two conditions are "in association." The patient has tuberculosis in association with pregnancy, or a cold in the head in association with an ingrowing toe-nail. Why not just plain "and"?

I am sure we could each compile our favourite list of overworked and ill-treated words and phrases, and my own would certainly include "marked tendency," "haemorrhagic episode," "predisposition," and many others. But I should like to conclude with an example which creates for me a visual image of a charming and grateful little ceremony:

"To an experienced observer the patient presented the classical picture of typhoid fever."

By Goya, presumably.—I am, etc.,

Glasgow. BERNARD ISAACS.

POINTS FROM LETTERS

Treatment of Colds

Dr. J. L. KEARNS (London, W.12) writes: Pulv. penicillin and sulphathiazole *B.P.C.*, used as snuff from gelatin capsule size 000 containing about 5 grains three times daily for one or two days at the onset of dryness, tickling of nasal membranes, or sneezing, has had really remarkable results in aborting or cutting short the "head cold" onset. The capsule can be carried as prophylactic or at-hand treatment. Separating the parts of the capsule is readily done. The season is now propitious for extended trial, and I trust others will feel as gratified as I am with results.

Ayre's Tube or Safety-pin?

Dr. J. D. WHITBY (Newcastle-upon-Tyne) writes: I believe that the practice of putting a pin under the expiratory valve is more common than Dr. H. J. A. Simmons (September 15, p. 674) realizes. I have myself used it for two years. I cannot understand why he considers an Ayre's tube too small for children of the 6 to 10 age group. All that is required is a slightly larger tube. The only advantages of the safety-pin method are that it is simple and can be used for children or adults without alteration.

Early Recognition of Deafness

Mr. J. E. OLIVIER (McGill University, Montreal) writes: Professor A. G. Watkins states in his article on early recognition of congenital defects (September 22, p. 728) that "deafness is impossible to detect in the early months." I should like to call attention to a method of testing hearing in a young infant long before deafness is suspected through delay or difficulty in speech. This method uses the conditioned reflex mechanism. A jet of air is blown into the infant's eye causing a blinking response (the unconditioned stimulus). At the same time a bell is sounded (the conditioned stimulus). After several repetitions the bell alone will elicit the blinking response in a child with hearing, but not in a deaf one. This can be repeated so as to rule out coincidental responses.

Obituary

W. BROADBENT, M.D., F.R.C.P.

Dr. Walter Broadbent, consultant physician to the Royal Sussex County Hospital, died at his home at Henfield, Sussex, on October 17, aged 83. Walter Broadbent was the third son of the late Sir William H. Broadbent, Bt., K.C.V.O., M.D., F.R.S., who was a great authority on diseases of the heart. He was educated at Harrow School, Trinity College, Cambridge, and St. Mary's Hospital. After graduating M.B., B.Chir. in 1893 he held a number of resident posts at St. Mary's Hospital and at the Brompton Hospital. In 1896 he became a Member of the Royal College of Physicians, and a year later he proceeded M.D. He settled in practice in Brighton shortly afterwards, and he was elected to the staff of the Royal Sussex County Hospital in 1902. Carrying on the traditions of his distinguished father, whose life he wrote, he contributed many valuable articles to medical journals, mainly on diseases of the heart and lungs. During the first world war he spent some time in Italy and Southern Europe as a consulting physician to the Forces, and he much enjoyed the experience. In 1918 he was elected F.R.C.P.

At the Royal Sussex County Hospital his reputation as a physician was of the highest. His far-sightedness resulted in the establishment sixteen years ago of a department for the treatment of early nervous disorders: this was brought about through co-operation between the Lady Chichester Hospital for Early Nervous Disorders at Hove and the out-patient department of the Royal Sussex County Hospital. Broadbent was also on the staff of the Royal Alexandra Hospital for Children, and he was medical referee for cases of consumption to the Charity Organization Society, Queen Alexandra's Sanatorium at Davos, and the Royal National Hospital at Ventnor. He took a keen interest in the affairs of the British Medical Association, and was vice-president of the Section of Medicine at the Annual Meeting in 1913, as well as chairman of the Brighton Division in 1923–4 and president of the Sussex Branch in 1928–9.

Dr. Broadbent will be long remembered not only for his outstanding medical ability and fine powers of diagnosis, but also for his wise and gentle thoughtfulness, his love of a good story, and his interest in sport. A member of the Leander Club, in his younger days he was a good oarsman, being in the First Trinity first boat in 1889–90, and he rejoiced in winter sports in Switzerland.

He married Edith Monroe, daughter of the Rt. Hon. John Monroe, P.C., and had two sons and two daughters, who all survive him. Mrs. Broadbent was aided and abetted in her public work by her husband; she was made O.B.E. in 1928.

As a result of a serious motor accident Dr. Broadbent found it difficult to get about recently, but with abounding pluck and determination he succeeded. Only two days before he died he was out in the garden with his spud for weeds. This courage he showed throughout his life. He was deeply appreciated by his colleagues and was the best and most unselfish of friends.—A.H.A.B.

Dr. Nelson West Jenkin died at his home in Hindhead on September 26, aged 69. He was educated at Giggleswick School, Christ's College, Cambridge, and St. Thomas's Hospital. After qualifying in 1908 he was appointed house-physician and later resident anaesthetist and senior resident house-physician at St. Thomas's. In 1909 he joined a partnership at Hindhead and practised there for 42 years. He built up a large practice, as a man of his character, professional knowledge, and devotion to duty was bound to do. In the first world war he served in France and later in the hospital ship *Egypt*. After demobilization he took the degrees of M.B., B.Ch. During the second world war he was senior medical officer at the Haslemere and District Hospital, and gave up the greater part of his spare time to running and organizing this hospital on a war basis. His outside interests were many, but his patients always came first. He was a good athlete, a member of his school Rugby fifteen, and the heavyweight of the fastest crew that Christ's College had ever had before his day or probably since. The crew rowed in the Grand Challenge Cup at Henley and reached the final of the Ladies Plate. In this crew he must have more than pulled his weight, and this he continued to do in everything he attempted throughout his life. He loved his garden and was a well-known expert on alpine plants. His holidays were spent in the mountains: he travelled as far afield as the Caucasus to search for rare plants. A winner of many prizes at the Royal Horticultural Society's shows, he introduced several species new to this country. He was an original member of the Alpine Society. In 1910 he married Mary Greaves, daughter of a Fellow of Christ's College. She died in May of this year. There were no children, and an adopted daughter, to whom he was most devoted, died aged 15 in 1928. Through life it seemed to fall to his lot to have to suffer more kicks and difficulties than are meted out to the average man. He bore his knocks with courage and cheerfulness and set a fine example to his patients. The last few years of his life were marred by a progressive loss of sight, and the last few months by a disease which he knew might at any time prove fatal. He had gradually to reduce his professional work, but he never allowed his physical disabilities to obtain mastery over his apparently unconquerable spirit. A large congregation at his funeral service, some of his old patients and friends coming from distant parts of England, gave proof of their affection and devotion.—R. E. G. G.

Dr. Herbert Melville Churchill died at his home in North London on October 11, aged 73. He qualified at the London Hospital in 1903, and two years later went to China as a medical missionary, working first at Kienning-fu and later (after an interval of service with the British Army in Salonika) at Foochow, where he taught surgery to Chinese students at the medical school. His knowledge of Chinese was such that he translated Caird and Cathcart's *Surgical Handbook* into that language. Returning home in 1919, he became secretary of the Medical Missionary Association. He entered general practice in Stoke Newington in 1923. Besides working hard as a general practitioner he found time to serve on the Borough Council, as well as on committees of the Church Missionary Society and the Egypt General Mission. After he retired from general practice he became first the secretary and then the chairman of the London committee for the King George V Memorial Hospital for merchant seamen in Malta. In this capacity his energy and organizing ability proved useful qualities. When the hospital was destroyed by enemy action during the war he began at once to plan for its rebuilding, visiting Malta twice (as a passenger in R.A.F. bombers) before the war was finished. After the war he raised the £100,000 needed, with the generous help of the Scottish Red Cross, and in spite of difficulties with permits, materials, and equipment the King George V Hospital was the first major building in the Mediterranean area to be reconstructed. Although often ill during the last three years, he remained at his work, and he drove himself to his office on the day before his death in order to attend a committee meeting. The Society for whom he worked and all who knew him best will long miss his experience and wisdom, coupled as they were with a rare unselfishness and personal humility.

Medico-Legal

"EXISTENCE" OF HOSPITALS UNAFFECTED BY N.H.S. ACT

[From Our Medico-Legal Correspondent]

By her will Miss Adah Phyllis Kelman, of Davenport, Cheshire, who died in 1947, left her residuary estate to be divided equally between "such of the Royal Manchester Children's Hospital, Pendlebury, the Christie Hospital and Holt Radium Institute, Withington, the National Trust, and St. Dunstan's, as shall at the time of division be in existence." On May 23, 1951, the executors of the will applied to the Chancery Division to solve the question whether the National Health Service Act had brought an end to the existence of the two hospitals.

Mr. Justice Romer[1] decided that the effect of the Act was to vest them in the appropriate bodies created by the statute, but that the change was one of management only. The charitable work of the hospitals was being carried on under the same names and in the same premises as before the Act, and he could not see why the change should determine the existence of the charity. He accordingly made a declaration that the bequest was effective, and that the two hospitals were for that purpose in existence.

[1] *Manchester Guardian*, May 24.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

Dr. John Hamill Crookston (Toronto) has been elected to an Elmore Medical Research Studentship, from October 1.

Professor James Dixon Boyd was elected into a Professorial Fellowship of Clare College on October 1.

Dr. L. B. Cole has been appointed deputy for the Regius Professor of Physic during Sir Lionel Whitby's term of office as Vice-Chancellor.

Dr. F. Howarth has been appointed deputy for the Sheild Professor of Pharmacology for the academic year 1951–2, the period during which Professor E. B. Verney, F.R.S., will be on leave of absence.

Dr. B. W. Davy has been appointed a Junior Health Service Officer with tenure from October 1 for three years.

Professor A. Leslie Banks, professor of human ecology in the University, has been elected to a Professorial Fellowship at Gonville and Caius College.

In Congregation on October 13 the following degrees were conferred:

M.B., B.Chir.—*D. G. Dickson, *E. J. Purcell, *M. F. Downey, Barbara M. Gray.

*By proxy.

UNIVERSITY OF ST. ANDREWS

At a Graduation ceremony held on October 12, the degree of B.L. was conferred on H. J. Gibson, M.B., Ch.B., D.P.H.

UNIVERSITY OF ABERDEEN

The following appointments are announced: *Lecturer in Surgery*, William Burnett, F.R.C.S. *Lecturer in Obstetrics and Gynaecology*, R. McF. Bernard, M.B., Ch.B., M.R.C.O.G. *Lecturers in Pathology*, R. C. Nairn, M.D., and A. W. Williams, M.D., D.C.P.

UNIVERSITY OF DURHAM

Sir Reginald Watson-Jones will deliver the tenth Rutherford Morison Lecture at the Royal Victoria Infirmary, Newcastle-upon-Tyne, on Tuesday, November 20, at 5.15 p.m. His subject is "Recent Progress in the Treatment of Fractures."

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending October 6 (No. 40).

Figures of notified *cases* are for: (*a*) England and Wales (London included) (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

Disease	1951 Week Ending October 6					1950 Corresponding Week					1942–50 England & Wales Corresponding Week		
	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	Highest	Median	Lowest
Diphtheria	30	1	16	—	2	40	6	11	6	5	988	319	40
Deaths	—	—	—	—	—	—	—	—	1	—			
Dysentery	124	33	62	1		187	14	149	1	2	390	207	63
Deaths		1		—			—		—				
Encephalitis, acute	15	—	—	—		4	—	—	—		4	1	—
Deaths		—			—		—			—			
Erysipelas			17	—	5			19	2	12			
Food-poisoning	125	16		2		416	22		1				
Infective enteritis or diarrhoea under 2 years				10	55				17	19			
Deaths	9		3	1	—	8		1	—	4			
Measles*	1,466	22	82	137	114	3,914	289	197	66	87	4,660	1,781	367
Deaths		—	—	—	—		—	—	—	—			
Meningococcal infection	27	4	13	1	1	30	3	13	2		54	32	24
Deaths		1	—				—	2					
Ophthalmia neonatorum	45	1	9	—		32	2	5	—		104	63	31
Pneumonia, influenzal	310	18	—	1	1	351	10	3	6		628	411	312
Deaths (from influenza)†	6	1	—	—	—	8	—	—	—	1			
Pneumonia, primary			135					134					
Deaths	109	16		5	6	131	18		12	4			
Poliomyelitis, acute:													
Paralytic	56	1	15	2	4	353	20	49	4	6	429	29	16
Non-paralytic	40	4											
Deaths§	7	—			—	25	1			1			
Puerperal fever			13					6					
Puerperal pyrexia‖	241	31	5	—		74	3	10	2	2	192	155	74
Scarlet fever	869	66	214	30	33	1,064	90	162	61	70	3,265	1,624	1,064
Deaths		—	—	—	—		—	—	—	—			
Smallpox	—	—	—	—		—	—	—	—				
Deaths				—					—				
(1) Tuberculosis, respiratory			136	43				136	41				
(2) Tuberculosis, non-respiratory			26	5				33	2				
(1) Deaths	113	15	21	4	8	136	21	15	4	8			
(2) Deaths		2	6	1	2		—	3	1	2			
Typhoid fever	9	—	—	—	—	10	2	2	1	—			
Deaths¶	—	—	—	—		1	—	—	—		36	26	14
Paratyphoid fever	31	—	2 (B)	2		11	2	1 (B)	1				
Whooping-cough	1,589	62	315	25	82	2,445	255	222	21	53	2,445	1,086	860
Deaths	1	—	—	—	—	4	1	—	—	—			
Deaths (0–1 year)	163	22	31	7	11	203	22	32	12	10	392	293	203
Deaths (excluding stillbirths)	3,996	650	550	87	140	4,529	681	546	105	145	4,529	4,051	3,826
Annual death rate (per 1,000 persons living)			11·3					11·0					
Live births	7,038	1,151	797	201	413	7,546	1,217	930	259	368	9,586	7,546	6,290
Annual rate per 1,000 persons living			16·3					18·7					
Stillbirths	184	24	34			147	15	20			253	200	147
Rate per 1,000 total births (including stillborn)			41					21					

* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The numbes of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

Vital Statistics

Outbreak of Meningitis

Cases of meningitis of unknown aetiology, similar to those in the outbreak in Durham (see this *Journal*, September 1, p. 555, and September 29, p. 862), are occurring in many different areas of the country, though now mainly in the south and to a less extent in the Midlands. Patients of all ages are affected, and all the cases run a benign course. Adults suffer more severe symptoms than children. A characteristic feature is that the train of infection is nearly always easily traced from person to person. In this respect the disease differs notably from poliomyelitis. Moreover, no cases with paralysis have been seen.

The chief symptoms are photophobia, vomiting and headache (severe in adults), raised cerebrospinal-fluid lymphocytes and protein, and muscle tenderness. In a few cases vesicles have been noted.

Laboratory investigations have so far failed to identify the causative agent. Coxsackie and mumps viruses are among the many that have been excluded.

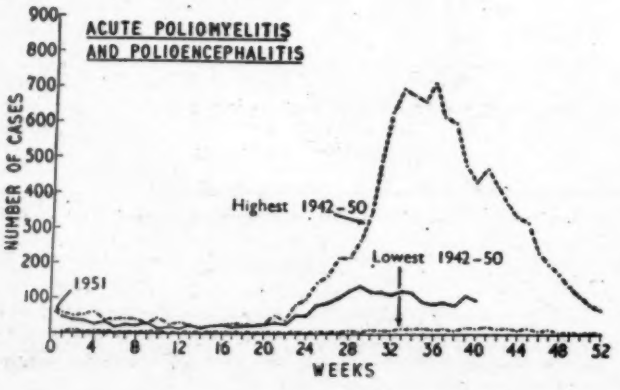
Food-poisoning in England and Wales

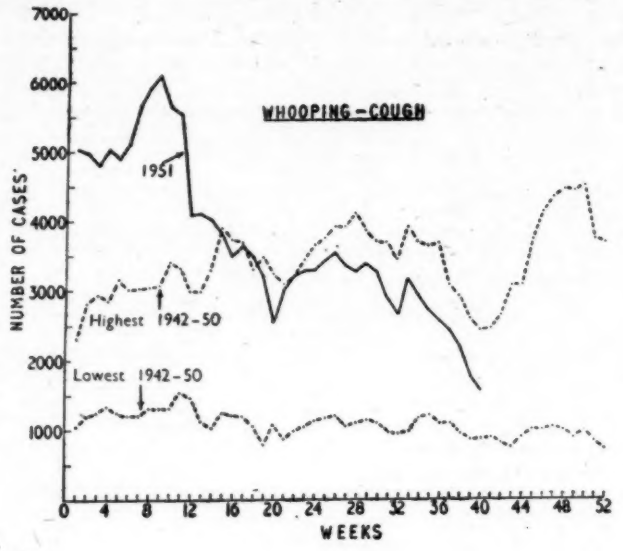
An analysis of the reports made during 1950 on food-poisoning has been published in the October issue of the *Monthly Bulletin* of the Ministry of Health and the Public Health Laboratory Service. The total number of incidents (outbreaks and sporadic cases) reported was 3,979, an increase of 64% over the number reported in 1949. Better reporting accounts for some of the increase, but on the evidence available it appears that food-poisoning is still increasing. The largest number of incidents was reported during the third quarter and the smallest in the first quarter. Salmonella infections accounted for the majority of the outbreaks; 1,564 were due to *Salm. typhi-murium* and 457 to other salmonellae, while in 1,807 the causal agent was unknown.

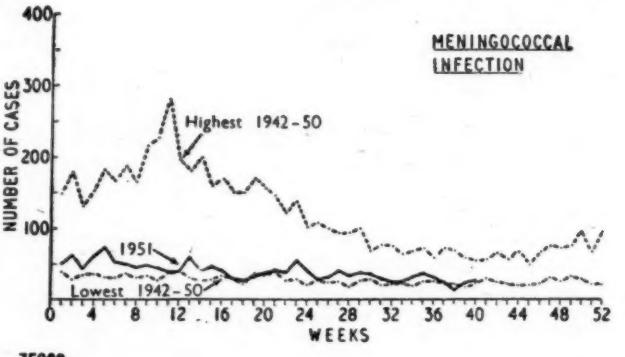
The foods known or considered most likely to have originated the outbreak were noted in 435 outbreaks. In 268 of these outbreaks meat dishes were mentioned, and in 78% of these incidents (48% of all incidents in which the food responsible was known) the outbreak was associated with processed or made-up meat such as pies, stews, sausage meat, brawn, pressed beef, reheated meat, rissoles, and cold meats.

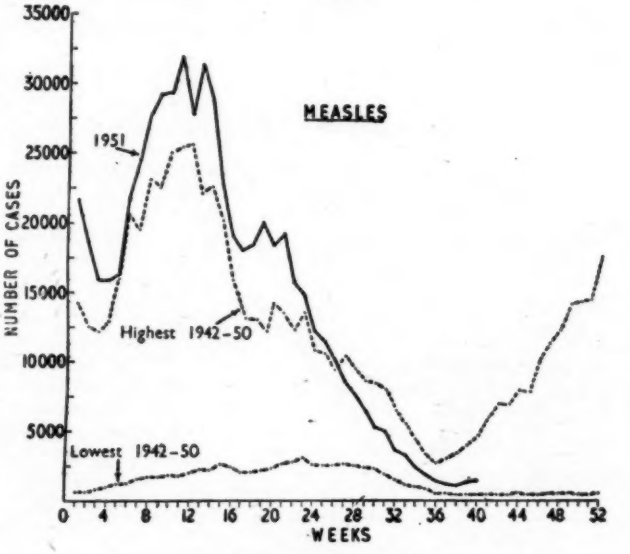
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus -------, the figures for 1951 thus ———. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

An increase was recorded in the number of notifications of measles 208, scarlet fever 128, and acute pneumonia 52 in England and Wales during the week ending October 6, while the only fall of any size was whooping-cough 180.

Half of the rise in measles was contributed by two counties, Staffordshire 67 and Warwickshire 61. The largest outbreaks in these counties were Stoke-on-Trent C.B. 52 and Warwick M.B. 71, and these outbreaks were, with the exception of Liverpool C.B. with 115 cases, the largest in the country. Very little change occurred in the local returns of scarlet fever. The rise in incidence was mainly due to a small rise throughout the northern section of the country; the largest increase was 33 in Lancashire. A small fall in the number of notifications of whooping-

cough was recorded in every region of the country; the largest decrease was Yorkshire West Riding 45. The notifications of diphtheria were 5 more than in the preceding week, but no change of note occurred in the local returns. Of the 31 cases of paratyphoid fever, 12 were notified in Lancashire.

The number of notifications of paralytic acute poliomyelitis were 8 fewer, and of non-paralytic cases 4 fewer, than in the preceding week. The largest returns during the week were Yorkshire West Riding 20 (Sheffield C.B. 4), Lancashire 13 (Middleton M.B. 3), and London 5.

Twenty fewer cases of dysentery were notified during the week reviewed than in the previous week. The largest centres of infection were London 33 (Islington 8), Surrey 16, Lancashire 11, Middlesex 9.

Poliomyelitis

Poliomyelitis notifications in the week ending October 13 were as follows (figures for the previous week in parentheses): paralytic, 54 (56); non-paralytic, 40 (40); total, 94 (96).

The table below compares the number of notifications in the current year up to and including the week ending October 13 (41st week) with the corresponding period for the preceding four years:

Years	Cases
1947	7,458
1948	1,625
1949	4,486
1950	7,019
1951	2,389

Week Ending October 13

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,032, whooping-cough 1,612, diphtheria 41, measles 1,648, acute pneumonia 395, acute poliomyelitis 94, dysentery 118, paratyphoid fever 90, and typhoid fever 6.

Medical News

N.A.P.T. Christmas Seals

For many years the N.A.P.T. Christmas seals have been provided by the Canadian Tuberculosis Association, but this year they have been printed in England from a design by a patient. The idea of a Christmas seal campaign to raise money for tuberculosis sufferers was started in Denmark over 50 years ago, and has since been used in many countries. The proceeds from the sale of seals provide the chief income of the association, enabling it to carry out its social welfare work. The sale opened on October 22, and will continue until Christmas; the seals cost 4s. per 100, and may be obtained from the Duchess of Portland, N.A.P.T., Tavistock House North, W.C.1. Christmas cards in the same design may also be obtained, price 6s. per dozen.

Chelsea Clinical Society

The first meeting of the 55th session was held on October 9 at the South Kensington Hotel, S.W.7, with the president, Dr. J. H. Dunn, in the chair. A discussion on "Some Medical Problems in High Speed and Altitude Flying" was opened by Group Captain W. K. Stewart, a film being shown, and a further contribution on "Medical Problems of Civil Aviation," by Dr. J. E. Gabb, gave an insight into some of the problems faced by the air line companies in the safe transit of passengers. The next meeting will be on November 14.

European Society of Cardiovascular Surgery

A European Society of Cardiovascular Surgery has been established under the presidency of Professor René Leriche, of Paris. The vice-president is Professor Raynaldo Dos Santos, of Lisbon, and the secretary Dr. Georges Arnulf, of Lyon. The first meeting of the Society will be held in Strasbourg next year on October 3 and 4, when the subject to be discussed is "Chronic Arterial Obliteration, with the Exception of Aneurysm and Embolism." The proceedings of the meeting will be published in full.

Will anyone who is interested in membership of the Society, the annual subscription to which is 5,000 French francs, communicate with Sir James Learmonth, Department of Surgery, University New Buildings, Edinburgh, 8, who was asked to undertake the duties of British delegate at the meeting.

Walter Reed Centenary

The 100th anniversary of Walter Reed's birth was commemorated in a striking way by the Osler Club, which on October 12 staged a symposium in his honour on "Man's Experiments on Man." Dr. G. W. M. Findlay, in his opening address, mentioned that Reed's 100th birthday coincided with the jubilee of his announcement that yellow fever is transmitted by the bite of the mosquito *Aëdes aegypti*. He paid tribute to the eight doctors and one technician who gave up their lives in the cause of science, and briefly but graphically described his own investigations. Dr. Ancel Keys, director of the laboratory of physiological hygiene, University of Minnesota, commented on the excellent designing and execution of Reed's experiments long before the introduction of controlled trials, gave an amusing account of the limitations and virtues of human experiments, and briefly sketched the Minnesota experiment on human starvation. The symposium was brought to a conclusion by Dr. J. L. Burn, M.O.H. for Salford, who showed a filmstrip of Walter Reed and gave an account of the Sheffield experiments on vitamin-A deficiency, in the course of which some conscientious objectors developed pulmonary tuberculosis, worthily upholding the Reed tradition. Dr. Hugh Sinclair, in the discussion, told the story of Dr. William Stark, who in 1766 put himself on a highly purified diet and to his intense delight developed scurvy, which he cured with blackcurrants. A subsequent experiment, however, ended fatally when, on the advice of Sir John Pringle, he took salt as an "antiscorbutic."

British American Hospital in Madrid

The secretary of this hospital has written to draw attention to its existence as a small (seven-bed) voluntary hospital supported by the Anglo-American community in Madrid to provide British and American nursing standards for themselves and for visiting tourists and businessmen who may fall ill while in Spain. Dr. McLellan, who is the doctor at the British Embassy, is in charge.

Emergency Bed Service: Applications and Admissions

During the seven days ending October 22 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 856, of whom 88.43% were admitted.

Wills

Dr. Robert Smerger Albert Drought left £27,541. He left £1,000 to the Royal Medical Benevolent Fund.

COMING EVENTS

Leeds School of Medicine Annual Dinner

The annual dinner of past and present students of Leeds School of Medicine will be held at the Great Northern Hotel, Leeds, on Friday, November 30, at 7 for 7.30 p.m., when the guest of honour will be Sir Geoffrey Jefferson, F.R.S., professor of neurosurgery in the University of Manchester. Full particulars may be obtained from Mr. H. K. Beardwood, honorary secretary of the Students' Representative Council, School of Medicine, Leeds, 2.

St. Thomas's Hospital Ball

The annual ball will be held at the Dorchester Hotel, Park Lane, London, W.1, on Thursday, November 15, from 9 p.m. to 2 a.m. Double tickets (price 60s.) may be obtained by post, enclosing an appropriate cheque (payable to the St. Thomas's Hospital Ball Committee and crossed), from Mr. R. Ross Russell, St. Thomas's House, Lambeth Palace Road, London, S.E.1.

Airborne Medical Society

The annual meeting and dinner of the Society will be held in Edinburgh on March 15, 1952 (Saturday)—i.e., the night of the England *v.* Scotland rugby match. This will be the tenth anniversary of the foundation of the Society. Further particulars may be obtained from Dr. A. A. Eagger, Slough Industrial Health Service, Farnham Road, Slough, Bucks.

Contraceptive Technique

A lecture and demonstration (on living models) on contraceptive technique will be given by Marie C. Stopes at the Mothers' Clinic, 108, Whitfield Street, London, W., on Thursday, November 1, at 2.30 p.m. Tickets must be obtained in advance, as space is limited.

B.M.S.A. Lecture, Cardiff

The annual B.M.S.A. lecture for 1951 will be delivered by Professor H. L. Sheehan at 5.15 p.m. on Thursday, November 8, in the Pathology Lecture Theatre, Cardiff Royal Infirmary. The subject of the lecture will be "The Diagnosis and Treatment of Hypopituitarism." All medical practitioners are cordially invited to attend.

North-east Metropolitan Registrars Group

The annual general meeting of the North-east Metropolitan Regional Registrars Group will be held at B.M.A. House, Tavistock Square, London, W.C., on Thursday, November 8, at 8 p.m. All senior registrars and registrars in the region are invited to attend.

Symposium on the "Suprarenal Cortex" at Bristol

The Colston Research Society's 1952 symposium will be held from March 31 to April 4, 1952, and the provisional list of guest speakers includes Professor F. Verzar (Basle) on the nature of adrenal cortical secretion, Dr. George W. Thorn (Harvard) on the clinical applications of A.C.T.H. and steroid hormones, Dr. C. H. Li (Berkeley, Calif.) on the preparation and assay of A.C.T.H., Dr. Harry Robinson (Merck), Dr. Dwight J. Ingle (Upjohn Company), and Dr. Hudson Hoagland (Worcester, Mass.), as well as a number of British workers. Those interested in attending the symposium should write to Professor J. M. Yoffey, Department of Anatomy, the University, Bristol, 8, or to Dr. J. S. Baxter, the symposium secretary, at the same address.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday

●INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., October 29, 11 a.m., "*Female Gonorrhoea,*" by Dr. W. N. Mascall.

MEDICO-LEGAL SOCIETY.—At 26, Portland Place, London, W., October 29, 8.15 p.m., "*Some Aspects of the Law of Defamation,*" presidential address by the Hon. Mr. Justice Slade.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND: FACULTY OF ANAESTHETISTS, Lincoln's Inn Fields, London, W.C.—October 29, 5 p.m., "*Anaesthetic Drugs,*" by Dr. A. H. Galley; 6.15 p.m., "*Autonomic Drugs,*" by Dr. H. C. Stewart.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—October 29, 5 p.m., "*Congenital Fundus Lesions,*" by Professor Arnold Sorsby.

Tuesday

BRISTOL UNIVERSITY.—At Large Lecture Theatre, Wills Physics Building (Royal Fort), October 30, 8.15 p.m., "*The Physical Principles of Radioactivity and the Release of Atomic Energy,*" 40th Long Fox Memorial Lecture by Professor C. F. Powell, F.R.S.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., October 30, 5.30 p.m., "*Biochemical Function of Vitamin B*$_{12}$," by Professor R. A. Peters, F.R.S.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—October 30, 5.30 p.m., "*The Value and Limitations of Sex Hormones in Dermatology,*" by Dr. H. W. Barber.

●INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., October 30, 11 a.m., "*Cardiovascular Syphilis,*" by Dr. E. G. B. Calvert.

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.—October 30, 5 p.m., First Langdon-Brown Lecture, written by the late Dr. A. Geoffrey Evans, will be read by the President.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND: FACULTY OF ANAESTHETISTS, Lincoln's Inn Fields, London, W.C.—October 30, 5 p.m., "*Anaesthetic Drugs,*" by Dr. A. H. Galley; 6.15 p.m., "*Autonomic Drugs,*" by Dr. H. C. Stewart.

Wednesday

DAVIDSON CLINIC, 58, Dalkeith Road, Edinburgh.—October 31, 8 p.m., "*Psychology and Freudian Analysis,*" by Dr. Laetitia Millard.

EDINBURGH CLINICAL CLUB.—October 31, 4 p.m., clinical meeting by Dr C. W. Graham. Visit to the Eye Department, Edinburgh Royal Infirmary

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—October 31, 5.30 p.m., "*Mycology—Microsporon Infections,*" by Dr. R. W. Riddell.

●INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., October 31, 11 a.m., "*Tertiary Syphilis,*" by Dr. W. N. Mascall; 4.30 p.m., "*The Pathology of Calculus Disease,*" by Dr. C. E. Dukes.

OXFORD UNIVERSITY.—At Radcliffe Infirmary, Oxford, October 31, 5 p.m., "*Maternal Obesity,*" Litchfield Lecture by Dr. J. H. Sheldon.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND: FACULTY OF ANAESTHETISTS, Lincoln's Inn Fields, London, W.C.—October 31, 5 p.m., "*Anaesthetic Drugs,*" by Dr. A. H. Galley; 6.15 p.m., "*Analeptics,*" by Dr. H. C. Stewart.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—October 31, 5 p.m., "*The Response of the Body to a Wound,*" Hunterian Lecture by Professor E. D. Churchill (Harvard University).

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, London, W.—October 31, 3.30 p.m., "*Burns and Scalds Among Children*" *(Illustrated),* by Mr. D. M. Jackson.

Thursday

BIRMINGHAM UNIVERSITY MEDICAL SOCIETY.—November 1, 5 p.m., "*The Pathology of Calculous Disease of the Kidney and Bladder,*" B.M.A. Lecture by Dr. Cuthbert Dukes.

GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY, The Union, University Avenue, Glasgow.—November 1, 7.30 p.m., address by Professor A. Ritchie.

HONYMAN GILLESPIE LECTURE.—At University New Buildings (Anatomy Theatre), Teviot Place, Edinburgh, November 1, 5 p.m., "*Surgical Emergencies of Infancy,*" by Mr. F. H. Robarts.

●INSTITUTE OF CHILD HEALTH, Hospital for Sick Children, Great Ormond Street, London, W.C.—November 1, 5 p.m., "*The Disorders of Sleep,*" by Professor R. S. Illingworth.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—November 1, 5.30 p.m., "*Histopathology—Tumours of Skin Appendages,*" by Dr. H. Haber.

●INSTITUTE OF UROLOGY.—At St. Paul's Hospital, Endell Street, London, W.C., November 1, 11 a.m., "*Treatment of Syphilis,*" by Dr. W. N Mascall.

LONDON UNIVERSITY.—At Royal Society of Medicine, 1, Wimpole Street, W., November 1, 5 p.m., "*Articulatory Defects in Aphasia,*" Semon Lecture by Dr. Macdonald Critchley.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND: FACULTY OF ANAESTHETISTS, Lincoln's Inn Fields, London, W.C.—November 1, 5 p.m., "*Local Anaesthetics,*" by Dr. A. H. Galley; 6.15 p.m., "*Digitalis and Quinidine,*" by Dr. H. C. Stewart.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—November 1, 5.30 p.m., "*Anaesthetics in Ocular Surgery,*" by Dr. J. H. Willis.

ROYAL SOCIETY, Burlington House, Piccadilly, London, W.—November 1, 4.30 p.m., "*Functional Transplants of the Anterior Pituitary Gland,*" by Dr. G. W. Harris and Miss Dora Jacobsohn; "*Neuronal Transport of the Virus of Mouse Encephalomyelitis,*" by Mr. F. K. Sanders.

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, London, W.—November 1, 5 p.m., "*Articulatory Defects in Aphasia,*" by Dr. Macdonald Critchley.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—November 1, 4.30 p.m., lecture-demonstration in neurology by Dr. D. Williams.

UNIVERSITY COLLEGE, Gower Street, London, W.C.—November 1, 5 p.m., "*The Law of Abortion,*" by Professor Glanville Williams.

Friday

British Postgraduate Medical Federation.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., November 2, 5.30 p.m., "*Metal Catalysis and Intracellular Respiration*," by Professor D. Keilin.

●Institute of Dermatology, Lisle Street, Leicester Square, London, W.C.—November 2, 5.30 p.m., clinical demonstration by Dr. H. W. Barber.

●Institute of Urology.—At St. Paul's Hospital, Endell Street, London, W.C., November 2, 11 a.m., "*Lymphogranuloma Inguinale, Granuloma Venereum, and Condylomata Accuminata*," by Mr. A. H. Harkness.

●Postgraduate Medical School of London, Hammersmith Hospital, Ducane Road, W.—November 2, 2 p.m., "*Acute Haematogenous Osteomyelitis*," by Mr. C. W. Fleming; 4 p.m., "*Antibiotics in Infectious Diseases*," by Dr. H. Stanley Banks.

●Royal College of Surgeons of England: Faculty of Anaesthetists, Lincoln's Inn Fields, London, W.C.—November 2, 5 p.m., "*Drugs Acting on Blood and Blood Formation*," by Dr. H. C. Stewart; 6.15 p.m., "*Drugs Acting on the Urinary Tract*," by Dr. H. C. Stewart.

Royal Eye Hospital, St. George's Circus, Southwark, London, S.E.—November 2, 4.30 p.m., "*Points in the Selection, Testing, Maintenance, and Use of Ophthalmic Instruments*," by Mr. A. J. Cameron.

Royal Medical Society, 7, Melbourne Place, Edinburgh.—November 2, 8 p.m., "*The Treatment of Pulmonary Tuberculosis*," by Mr. W. A. Mahon.

APPOINTMENTS

British Railways (London Midland Region).—*Assistant Medical Officers*, J. T. Crean, M.R.C.S., L.R.C.P., F. L. Davies, M.R.C.S., L.R.C.P., and I. M. Ramsden, M.B., Ch.B.

Cockburn, William, M.B., Ch.B., D.M.R.D., Consultant Radiologist, Scottish Borders Hospital Group, Peel Hospital, near Galashiels.

East Anglian Regional Hospital Board.—*Assistant Anaesthetist (S.H.M.O. status) in Wisbech, Doddington, and Peterborough Area*, J. K. Black, M.B., B.Ch., D.A. *Anaesthetic Registrar, East Suffolk and Ipswich Hospital*, J. P. Kwella, M.D. *Medical Registrar, Newmarket General Hospital*, F. Starer, L.R.C.P.&S.Ed. *Gynaecology and Obstetrics Registrar, Peterborough and District Memorial Hospital*, H. Rees, M.B., B.Ch., D.Obst.R.C.O.G. *Psychiatric Registrar, St. Andrew's Mental Hospital, Thorpe, Norwich*, Dorothy M. J. Emslie, M.B., Ch.B. *Senior Orthopaedic Registrar, United Norwich Hospitals*, S. W. Davidson, M.B., Ch.B., F.R.C.S.Ed *Registrar in Dermatology, Norfolk and Norwich Hospital*, C. F. Bunting, M.R.C.S., L.R.C.P.

Fraser, D. J., M.B., Ch.B., D.P.H., Medical Officer, Central District, and Assistant County Medical Officer, County of Flint.

Hospital for Sick Children, Great Ormond Street, London, W.C.—*Two Medical Registrars and Pathologists (Senior Registrar Grade)*, J. A. Black, M.D., M.R.C.P., P. J. N. Cox, B.M., B.Ch., M.R.C.P., D.C.H. *Two Part-time Registrars to the Department of Physical Medicine (Registrar Grade)*, J. Luder, M.D., M.R.C.P., D.C.H., G. R. Parry, M.B., B.S. *Three House-physicians (Senior House Officer Grade)*, T. E. Oppé, M.B., B.S., M.R.C.P., D.C.H., Constance C. Forsyth, M.D., M.R.C.P., H. G. Rischbieth, M.B., B.S., M.R.A.C.P. *House-surgeon (Senior House Officer Grade)*, Kathleen A. M. Frith, M.B., B.S.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Arnott.—On October 19, 1951, at the Queen Elizabeth Hospital, Birmingham, to Dorothy (formerly Hill), wife of W. Melville Arnott, M.D., F.R.C.P., a son.

Finigan.—On October 10, 1951, at King's College Hospital, to Mari (formerly Williams), wife of Dr. F. O'D. Finigan, a daughter.

Innes.—On October 13, 1951, at Edinburgh, to Dr. Elizabeth Marion (formerly Elma Hislop), wife of Dr. James Innes, a daughter.

Ledingham.—On October 18, 1951, in London, to Josephine (formerly Metcalf), wife of Dr. J. M. Ledingham, a son.

Levi.—On October 8, 1951, at Liverpool Maternity Hospital, to Dr. Pearl Levi (formerly Lyons), wife of Dr. H. T. Levi, a daughter—Sylvia Ruth.

Puszkiewicz.—On September 28, 1951, to Gertruda, wife of Dr. R. Puszkiewicz, a daughter—Krystyna Maria.

Rainford.—On August 20, 1951, to Janet, wife of Dr. F. A. Rainford, Blyth Lodge, 35, London Road, Bromley, Kent, a daughter.

DEATHS

Anning.—On October 11, 1951, at Johannesburg, South Africa, Charles Clifford Paul Anning, C.B.E., M.R.C.S., L.R.C.P., D.P.H.

Bingham.—On October 14, 1951, Sydney Oliphant Bingham, M.R.C.S., L.R.C.P., of The Lane House, Shirland, Derbyshire.

Donovan.—On October 15, 1951, at his home, William Terence Donovan, M.B., Ch.B., D.P.H., aged 52.

Griffiths.—On October 15, 1951, John Howell Griffiths, M.D., D.P.H., of 55, De Lisle Road, Bournemouth.

Henry.—On October 14, 1951, at Epsom County Hospital, Gordon Campbell Henry, M.B., B.S., of 90, Manor Drive, Ewell, Surrey.

Mackichan.—On October 18, 1951, at a nursing home, Francis William Mackichan, M.B., Ch.B., of Vicars Drive, Rochdale, Lancs, aged 67.

Pain.—On October 16, 1951, at a nursing home, Arthur Pain, M.R.C.S., L.R.C.P., late of Thorney, Cambs, aged 80.

Thompson.—On October 2, 1951, at 29, Rutherford Road, Liverpool, Herbert Marshall Thompson, M.B., Ch.B., aged 69.

Way.—On October 16, 1951, at "The Warren," Compton Down, near Winchester, Hants, Arthur Orsborn Way, M.R.C.S., L.R.C.P., aged 82.

Weir.—On October 12, 1951, at a nursing home, Jersey, Edmund George Harrison Weir, M.D., of Fernlea, St. Clement, Jersey, C.I., late of Malacca, Malaya, aged 74.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

"Antabuse" and Anaesthetics

Q.—*When a patient is receiving antabuse for the treatment of chronic alcoholism, symptoms of some severity develop if he resorts to alcohol. Is ethyl alcohol the only intoxicant to which he is sensitized by antabuse? May a general anaesthetic be administered with safety to a patient who is undergoing antabuse treatment?*

A.—When patients taking antabuse (tetraethylthiuram-disulphide) consume alcohol they experience very unpleasant sensations, such as flushing, palpitations, and nausea, due to increased oxidation of the alcohol to acetaldehyde. The symptoms can be produced in normal subjects by injecting acetaldehyde intravenously. Normally, a small amount of the latter is found in the blood after consuming alcohol; it is increased about tenfold if antabuse is given previously.

Anaesthetics can be given to a patient undergoing antabuse treatment if it is borne in mind that in some patients its use may be accompanied by a fall in blood pressure. In such cases spinal analgesia would be contraindicated. The use of cyclopropane would also appear to be unwise owing to the possible production of cardiac irregularities. Bromethol should not be administered, as it forms bromacetaldehyde on oxidation and might therefore intensify the reactions from antabuse. There is no objection to the use of other anaesthetic agents.

"Salt-free Diet"

Q.—*Could you advise me how to give variety to a salt-free diet and make it appetizing? Please include a sample menu in your answer. Are the proprietary sauces, such as "H.P." and "Worcester," salt-free?*

A.—The success of a low-salt diet in the treatment of congestive heart failure and other oedematous states depends primarily upon adequate restriction of dietary *sodium*. For this reason the term "low-sodium diet" is to be preferred. Sodium restriction may be mild, moderate, or severe, and to achieve these degrees of restriction diets may be prepared which limit sodium intake in 24 hours to 1.5–3 g., 0.5–1.5 g., and less than 0.5 g., respectively.

In general practice mild or moderate low-sodium diets will usually be found adequate. They are simple to prepare, may be varied often, and can be prescribed for long periods. Diets containing less than 0.5 g. sodium are usually reserved for hospital patients with obstinate cardiac oedema which resists rest, digitalis, and mercurial diuretics. Such diets are difficult to prepare, and they are usually prescribed for short periods only. They are dull and monotonous; variation is strictly limited, and few patients will tolerate them for long periods. In addition, the patients need close supervision; for, if mercurial diuretics are given simultaneously and fluids restricted, the risk of uraemia is a real one.

Mild sodium restriction may be achieved without inconvenience to the busy housewife by observing the following points. Avoid: salt at table; salt-preserved foods—e.g., cheese, ham, bacon, salted fish, olives, sausage of any kind; highly salted foods—e.g., salted nuts and potato chips; relishes—e.g., H.P. and Worcester sauce, pickles, ketchup—all of which have a high sodium content. For *moderate* sodium restriction the following foods must also be avoided: salt in any kind of cooking; canned vegetables, meat, or soup; frozen peas or frozen fish fillets; fruits preserved with

sodium benzoate; shellfish, except oysters. *Severe* sodium restriction involves all the above limitations and, in addition, the use of salt-free bread, butter, or kosher margarine, and milk should be restricted to half a pint daily. Any foods made with baking-powder, soda, or prepared flour, also beer and stout, should be forbidden.

Low-sodium diets tend to be dull and monotonous because they are tasteless. Meals may be made appetizing by varying the menu and by the skilful use of herbs and seasoning in cooking—e.g., sage and onion with pork served with spiced apple sauce. The frequent use of mustard and vinegar, particularly in the preparation of mayonnaise and salad dressing, will also do much to counteract the tastelessness of a low-sodium diet. Salt substitutes are not advised.

Menu

Breakfast.—Fruit juice and/or stewed prunes. Egg or fish. (Unsalted) buttered toast and jam or marmalade. Weak tea or coffee with sugar.

Lunch.—Egg, home-made unsalted cream cheese, meat, fish, poultry, or rabbit Vegetables. (Unsalted) bread and butter. Jelly, pastry, or fruit.

Dinner.—Vegetable soup, baked potato, protein food as at lunch. Vegetables or salad. (Unsalted) bread and butter. Baked apple and custard. Black coffee.

Reference

Proudfit, F. T., and Robinson, C. H. (1946). *Nutrition and Diet Therapy*. Macmillan, New York.

Preservatives and the E.S.R.

Q.—*When I ordered some 3.8% sodium citrate for E.S.R. estimation it was delivered containing 0.1% chlorocresol. Is this addition likely to interfere with the accuracy of the estimation?*

A.—Having no idea whether chlorocresol will affect the E.S.R., we have tried it out and found that it does increase the rate slightly. It seems to act by increasing rouleaux formation, and it might give fallacious readings in anaemic patients. It seems, therefore, that the simple 3.8% sodium citrate solution should be used for E.S.R. estimations, and the addition of preservative avoided.

Persistent Cough after Virus Pneumonia

Q.—*What are the likely causes of an unproductive cough persisting for six months after a virus pneumonia? The lung fields are clear radiographically. Is too much exposure to sun a factor?*

A.—It is very uncommon for structural abnormalities of the lungs to persist after a virus pneumonia has cleared up. This makes it probable either that the virus pneumonia was complicated by other organisms or that other causes are factors in the persistence of the cough. These may be intrabronchial obstructions, pressure on the bronchus from outside, or sinus infections. These possibilities should be investigated, if necessary by bronchoscopy. It is almost inconceivable that excessive exposure to sun should be a factor.

Shock and Disseminated Sclerosis

Q.—*Does mental shock or physical injury play any part in precipitating the onset of disseminated sclerosis?*

A.—The relationship of the onset of disseminated sclerosis to a preceding mental shock or physical injury is largely a matter of opinion. The majority of neurologists to-day would probably agree, however, that an emotional upset and also physical trauma may at times appear to predispose towards the development of signs and symptoms of this disease or of a relapse. To support the contention of attributability, however, it is probably necessary to satisfy oneself that the injury or shock is of adequate severity. In other words, a trivial upset or injury can seldom be held responsible. Secondly, the interval between the shock or injury and the onset of the disease must not be too long—i.e., it should not be more than a matter of some days.

Poor Peripheral Circulation in a Child

Q.—*What treatment is recommended for a child of 15 months with a poor peripheral circulation? The child's extremities are cyanosed, swollen, and, in cold weather, blistered.*

A.—It is easier to treat the symptoms due to a poor peripheral circulation than the cause, which is often difficult to define precisely.

Differential Diagnosis.—In pink disease the extremities are, as the name describes, pink; but there is often lividity and some cyanosis as well. They may be swollen and even oedematous, and there is often blistering and peeling. The essential diagnostic feature is that the hands and feet are clammy and cold most of the time, due to the capillary dilatation, sweating, and evaporation. Circulation is flushed but not stagnant. Raynaud's disease is very rare in childhood. The essential feature is paroxysmal cyanosis gradually getting worse and tending to go on to blanching, often precipitated by emotion. Gangrene is sometimes seen. Acrocyanosis is a name rather than a disease. There is a generally poor peripheral circulation which naturally shows most in the hands and feet. On exposure to cold thrombosis of arterioles may occur, giving rise to chilblains. These may be necrotic in the centre or surmounted by a blister in the early stage. Acrocyanosis is sometimes seen without coldness of the extremities. The cyanosis varies in intensity, but is seldom completely absent.

Treatment.—Marked changes of skin temperature should be avoided. The bed should be warmed before putting the child in it, and long, loose bedsocks should be worn. During the day loose woollen clothing, not tight or felted, should be worn, and mittens indoors. Before going out of doors the child should spend some time in overcoat, gaiters, etc., warming up. Chilblains require protection from trauma and infection. Diet and vitamins should be adequate, but the condition is not a manifestation of vitamin deficiency, and money should not be spent on giving extra quantities. The treatment of Raynaud's disease and pink disease may be found under textbook descriptions of these conditions.

NOTES AND COMMENTS

Recurrent Angioneurotic Oedema.—Dr. Morris Cutner (London, S.W.3) writes: May I supplement that part of the answer (October 13, p. 919) which refers to the treatment? Acting on a suggestion made by Dr. A. W. Frankland, of the Department of Allergy of St. Mary's Hospital, Paddington, we have, in the Department of Physical Medicine, since 1949, been carrying out investigations on the histamine ionization treatment of "allergic" symptoms (including angioneurotic oedema. Our observations tend to show that histamine ionization, with a 0.2% solution, at *weekly* intervals gives promising results. Treatment may have to be protracted, but appears to be worth while. A full account of the investigation will appear in the December issue of *Physiotherapy*.

Corrections

In the Refresher Course article on "Sprained Ankle" (October 20, p. 957), "flexor longus pollicis" (line 41 of the first column) should read "extensor pollicis longus."

In the report of a lecture to the Harveian Society, "Recent Advances in Endocrinology" (October 20), the statement starting on the eleventh line on page 966, "Pure growth hormone would probably prove more potent as a hypoglycaemic agent than cortisone," should read: "as an *anti*-hypoglycaemic agent."

All communications with regard to editorial business should be addressed to The Editor, British Medical Journal, B.M.A. House, Tavistock Square, London, W.C.1 Telephone: Euston 4499. Telegrams: *Aetiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
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